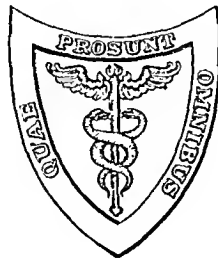


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VOL. CXLIII



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THE
AMERICAN JOURNAL
OF THE MEDICAL SCIENCES

JANUARY, 1912

ORIGINAL ARTICLES

THE CAUSES OF ASCITES: A STUDY OF FIVE THOUSAND
CASES.

By RICHARD C. CABOT, M.D.,

ASSISTANT PROFESSOR OF CLINICAL MEDICINE IN THE HARVARD MEDICAL SCHOOL, BOSTON.

I RECENTLY made a series of wrong diagnoses in cases of ascites. These failures, which were shared by some of the best diagnosticians in the country, suggested to me a study of the causes of this symptom. Until recently I had supposed that the diagnosis of the causes of ascites was one of the easiest in medicine. I was amazed to hear Dr. H. D. Rolleston say, in 1909, that he considered the diagnosis of cirrhosis a very difficult one; but in the light of recent events I have come to agree with him. To minimize the number of future mistakes, I have in this paper endeavored:

1. To tabulate from the autopsy records of the Massachusetts General Hospital the actual causes of ascites as found post mortem in 2217 autopsies (see Table I).

2. To tabulate the clinical diagnoses of ascites made at this hospital in the last forty years. Some of these diagnoses have been verified by operation or autopsy. A larger number rest on clinical evidence alone, but in most of the more dubious and more interesting cases we have operative or postmortem knowledge of the actual condition.

3. To tabulate the *rates* at which ascites accumulates in different diseases. Possibly these latter facts may be of some assistance in identifying through its more or less characteristic *tempo* of accumulation the ascites of tuberculous peritonitis.

4. To relate some of my failures and discuss the possibilities of better success in the future.

TABLE I.—Causes of Ascites as Found Post Mortem in 2217 Autopsies.

1. Cardiac weakness (due to valvular or parietal disease)	89	
2. Neoplasmic peritonitis	28	
Neoplasm of liver and glands	5	} 16 } 44
Neoplasm of stomach and glands	3	
Neoplasm of pancreas and glands	3	
Neoplasm of adrenal and glands	1	
Neoplasm of duodenum and glands	1	
Neoplasm of gut and glands	1	
Neoplasm of liver and omentum	1	
Hepatic lymphosarcoma	1	
3. Renal disease	26	
4. Cirrhosis of the liver	23	
5. Tuberculous peritonitis	10	} 15
Tuberculous adenitis (tabes mesenterica)	5	
6. Adherent pericardium	9	
7. Eclampsia	3	
8. Thrombosis of the cava	1	} 3
Thrombosis of the portal	1	
Thrombosis of the mesenteric	1	
9. Chronic fibrous peritonitis	3	
10. Uterine fibromyoma	3	
11. Intestinal obstruction	2	
12. Pancreatitis	1	
13. Ovarian cyst	1	
14. Acute yellow atrophy of the liver	1	
15. Status lymphaticus	1	
	224	

Table I shows the causes of fluid as found in the peritoneum in 2217 cases *at autopsy*. A quart or more of fluid was present in all these cases. Cases of septic peritonitis and hemoperitoneum are omitted. The bulk of the remaining cases are due, as was anticipated, to one of five causes: *Cardiac weakness, nephritis, abdominal neoplasms, cirrhotic liver and tuberculous peritonitis*.

I am uncertain whether the cases of adherent pericardium (all of which were associated with extensive peritoneal thickening) should be classed with the cases of cardiac weakness, or with those of chronic peritonitis. Of the other items in the list, the one most surprising to me is puerperal eclampsia.

CLINICAL STATISTICS OF ASCITES.

In some of the cases arranged in Table II the diagnosis was verified by operation or autopsy. This was the case with all the neoplasms and thromboses, and with most of the cases of intestinal obstruction and tuberculous peritonitis. But in the cardiac, renal, and hepatic cases and most of the blood diseases the evidence is wholly clinical.

Points of interest in this column are: (a) The frequency of ascites with ovarian cysts and tumors (see below, Table IV), and (b) the large figures obtained in intestinal obstruction. Probably in a considerable number of these cases the fluid may have been due to actual peritonitis associated with the obstruction.

In this table all the unstarred items represent cases actually studied in the original clinical record. The items which are starred were calculated as follows:

Throughout an eight year period I determined, by study of the clinical records, the percentage of ascitic cases among all the cases of cardiac and renal disease. These positive percentages were then applied to the total number of cases of each disease as shown by a count of the cards in the card catalogue (1870 to 1910). The starred items are, therefore, only approximately accurate.

TABLE II.—Causes of Ascites in 3086 Cases Observed Clinically at the Massachusetts General Hospital (1870–1910).

	Ascites present.	Per cent. showing ascites.	Ascites absent.	Total.
Myocardial weakness	694*	37	1183	1877
Mitral regurgitation	234*	22	1106	1340
Mitral stenosis and regurgitation	125*	24	399	524
Mitral and aortic regurgitation	72*	20	292	364
Aortic stenosis and regurgitation	87*	35	163	250
Aortic regurgitation	69*	29	169	238
Mitral stenosis	17*	8	200	217
Mitral and aortic stenosis and regurgitation	32*	42	45	77
Mitral and tricuspid regurgitation	67*	100	0	67
1. Total cases of cardiac weakness from all causes	1397*	28	3557	4954
2. Renal and cardiorenal	665*	29	1628	2293
3. Cirrhosis of the liver	325	88	42	367
4. Tuberculous peritonitis	263	82	58	321
5. Intestinal obstruction	86	43	113	199
6. Ovarian cyst, multilocular	31	7	360	391
7. Ovarian fibroma	10	50	10	20
8. Ovarian cancer	21	39	33	54
9. Ovarian sarcoma	1	20	4	5
10. Uterine fibroma	55	7	668	723
11. Neoplasmic peritonitis	53	82	11	64
12. Cancer of liver and lymphatic glands	30	20	118	148
13. Cancer of intestine and lymphatic glands	56	24	169	225
14. Cancer of pancreas and lymphatic glands	11	22	39	50
15. Malignant lymphoma (thoracic and abdominal)	5	50	5	10
16. Adherent pericardium	36	76	11	47
17. Pernicious anemia	15	7	199	214
18. Leukemia	12	13	76	88
19. Syphilis of the liver, etc.	4	40	6	10
20. Thrombosis (vena cava)	1	100	0	1
21. Thrombosis (portal)	1	100	0	1
22. Thrombosis (mesentery)	8	80	2	10
	3086		7109	10,195

Table III requires little explanation. The number of ounces of fluid between two exhaustive tappings is divided by the number of days intervening. There is a chance for error here in that the tappings, which were supposed to empty the peritoneal cavity, may, in fact, have left some fluid behind. But I do not think that this error is sufficiently serious to interfere with my results.

* Cases of ascites for the thirty-year period estimated by applying the known percentage during an eight-year period to the total number of cases.

I present herewith notes of 9 cases, illustrating some points of diagnostic interest and difficulty.

1. A case of cirrhosis without alcoholic history and with signs pointing rather to tuberculous peritonitis or cardiac dropsy.

2. A case of ovarian fibroma producing effusion in the belly and left chest; mistaken for tuberculous peritonitis.

3. A case very similar to the last, but turning out to be, in fact, tuberculous peritonitis.

4. A case of nephritis, in which the only symptom complained of was a rapidly recurrent ascites.

5. A case of fairly obvious cirrhosis; successful omentopexy.

6. A case first operated on for tuberculous peritonitis—none found. Later, cardiolysis was done for supposed pericardial cirrhosis. Slight improvement.

7. A case of supposed tuberculous peritonitis in a young girl. Tapping revealed mucilaginous fluid as from an ovarian cyst. Operation confirmed this.

8. Case of supposed splenic anemia with ascites. Prepared for operation. Evidence of syphilis found at the last moment. Disappearance of ascites and all other symptoms under Hg and KI.

9. Neoplastic peritonitis.

CASE I.—*Ascites and edema of legs, old pleurisy with marked displacement of the heart, epithelioma of lower lid; patient not alcoholic; death after operation; autopsy; cirrhosis and portal thrombosis.*

A housepainter, aged fifty-six years, who had taken alcohol only occasionally and in moderate amounts, noticed edema of his ankles seven weeks ago. A week later his belly swelled up, and he needed three tappings in six weeks, 8 or 9 quarts being withdrawn each time. Has lost 30 pounds in four months.

Examination. The right lower lid contained a small nodule showing all the characteristics of epithelioma. The heart was displaced so that its apex was in the anterior axillary line, while the right border of dulness was at the *left* sternal margin. There was a soft systolic murmur at the apex. The pulmonic second sound was not accentuated.

There was evidence of edema at the bases of the lungs. The belly contained a large amount of serous fluid, 250 ounces accumulating between two tappings sixteen days apart—an average of over 15 ounces a day. The fluids were 1006 and 1008 in gravity, and showed 80 per cent. and 90 per cent. of lymphocytes respectively in their sediments. Culture and animal inoculation negative. Fever was absent, and there was no reaction after the subcutaneous injection of 10 mg. of tuberculin.

There was some excess of neutral fat in the stools, suggesting to Dr. H. F. Hewes the stools of tuberculous peritonitis.

In diagnosis we considered cirrhosis of the liver, tuberculous peritonitis, and also the possibility that misplacement of the heart,

owing to pleural adhesions, might have kinked some one of the great abdominal veins so as to produce stasis and ascites.

Against cirrhosis was the early appearance of swelling in the legs and the moderate amount of alcohol ingested. Against tuberculosis was the negative tuberculin reaction and the low gravity of the fluid obtained by tapping. On the other hand, the cell count in the fluid, the appearance of the stools, as well as the old history of pleurisy, made tuberculous peritonitis a possibility. On the whole, cirrhosis seemed the more probable, and on operation, September 18, this was found.

The patient died September 29, and autopsy showed the ordinary lesions of cirrhosis of the liver, and in addition a thrombosis of the portal vein and a chronic peritonitis. There was also slight fibrous endocarditis of the aortic and mitral valves and slight hypertrophy and dilatation of the heart. There was obsolete tuberculosis of a tracheal lymph gland, which is interesting in view of the negative tuberculin reaction.

CASE II.—Effusion in the left chest and in the abdomen, with chronic cough, in a woman, aged thirty-eight years; loss of 20 pounds in weight; hypogastric tumor, believed to be uterine fibroid; operation showed fibroid of the ovary, no peritonitis; complete and lasting recovery.

A married woman, aged thirty-eight years, entered the hospital October 9, 1908. She has previously been well except that she has had a cough since she was a girl, and had typhoid fever ten years ago. For two or three years she has felt something wrong in the pelvis, and a year ago her doctor found a uterine fibroid there. The patient thinks this tumor has been present for four years.

Seven months ago she consulted a physician for pain in her left chest. He found pleural effusion, and withdrew 2 quarts of fluid by tapping. The same amount was withdrawn four weeks later, but the fluid again recurred.

A month ago the abdomen was noticed to be swelling, and this has increased up to the present time. She has had dyspnea on exertion for many years, but this has been worse within the last seven months, and now she cannot lie down flat. For the last two days the feet and legs have been swelling. The bowels move five to eight times a day during the last few weeks. Several examinations of the urine and several of the sputa have been negative.

Physical examination verified the findings of fluid in the left chest and in the abdomen. October 10 the abdomen was tapped and 18 pints of serum withdrawn. The specific gravity was 1018, and the cell count showed 63 per cent. of lymphocytes.

After tapping, a rounded solid tumor could be felt in the median line, apparently connected with the uterus, hard and painless. The diagnosis was believed to be tuberculous peritonitis, and the experiment was tried of withdrawing 8 ounces of fluid from the chest every two or three days, in order to prevent recurrence such as was

thought likely to follow if the whole amount was removed at once.

On November 21 the abdomen was again tapped and 18 pints again removed. This amount had accumulated in forty-two days, being at the rate of 7 ounces a day. After this tapping, pelvic examination showed a mass filling the pelvis, pushing the cervix up behind the pubes, very hard, irregular, non-elastic, and continuous with the suprapubic tumor. Dr. M. H. Richardson believed the condition to be one of tuberculous peritonitis with a concomitant uterine tumor, benign or malignant.

The association of fluid in the abdomen with fluid in the chest, and the history of a chronic cough, together with the high gravity of the fluid, made us confident of the diagnosis of tuberculous peritonitis, although in the two and one-half months of her stay in the medical wards there was never any fever. The blood and urine were throughout negative, as was the rest of the visceral examination.

Operation, December 12, showed no peritonitis, but a fibroma of the ovary; after the removal of this the patient convalesced rapidly, and when I saw her a year later she was in perfect health, as she had been for the last eleven months since leaving the hospital.

CASE III.—*Fluid in the abdomen and in one chest; general abdominal tenderness, soon passing off; positive reaction to tuberculin; no fever at other times; operation shows tuberculous peritonitis; presumable involvement of the pleura and of the left lung.*

An unmarried Italian girl, aged seventeen years, entered the hospital October 17, 1908, for enlargement of the abdomen, with fever and general abdominal pain. These symptoms had been present for the last two weeks, and had been accompanied by a dry cough.

On examination there was dulness and harsh breathing throughout the left lung except at the bottom of the axilla and the base posteriorly, where breathing was much diminished and resonance almost absent. Below the second left interspace were fine and medium crackling rales in front, and the same rales were heard below the angle of the scapula behind. The abdomen showed all the evidences of free fluid. Otherwise, physical examination was negative, and the blood and urine showed nothing abnormal.

After the first five days the patient had practically no fever throughout her two months' stay in the hospital. The abdomen showed general tenderness, but was otherwise negative, save for the evidences of free fluid above referred to. The abdomen was tapped on the 21st, and only a few ounces of clear serous fluid obtained. Five mg. tuberculin were injected subcutaneously on the 30th, after which the temperature rose from normal to 103.2° within six hours, returning to normal within twelve hours more. The cutaneous reaction for tuberculosis was also positive.

She gained weight, although there was no increase in the amount of fluid, and on November 12 was allowed to go home. After this she slept out of doors and lived out of doors continuously, but by January the abdomen began to enlarge again, and January 16 she was operated on and diffuse tuberculosis of the peritoneum found. Diagnosis was verified by microscopic examination of an excised piece. The Fallopian tubes were also tuberculous, and were removed. Convalescence was uneventful.

The resemblance between this case and that last described is striking. Indeed, but for the presence of the tumor in the first case, the abdominal tenderness and the scantiness of the ascites in the second, they are almost identical from a clinical standpoint, despite the entire difference of the acutal pathological condition present.

A relatively slow accumulation of fluid and a slight general rigidity and tenderness of the belly help to distinguish the ascites of tuberculous peritonitis from that produced by other diseases.

CASE IV.—Ascites and edema of the legs appearing as the only symptom in a boy, aged six years; urinary findings as of chronic glomerulonephritis; rapid reaccumulation of the fluid, necessitating tapping every two weeks; no other symptoms of importance.

A boy, aged six years, entered the hospital October 19, 1908. His history was not of significance up to five months previously, when his abdomen began to swell; there was also some puffiness of the face, but no other symptoms, and within a few weeks he was able to be up and about. Later, he relapsed, and two months ago the abdomen was tapped, 4 quarts of dark yellow, turbid fluid being withdrawn.

Since this there has been considerable vomiting, and at one time he had convulsions and was considered moribund. He was tapped again three weeks ago and 3 quarts of fluid withdrawn. Since then the abdomen has rapidly refilled.

On examination the heart impulse was in the nipple line, fourth space. The cardiac examination was otherwise not remarkable. Blood pressure not measured. The lungs were negative, the abdomen very prominent, showing all the evidences of free fluid. Considerable soft edema of the legs and feet.

The urine averaged between 5 and 10 ounces in twenty-four hours, during his stay in the hospital. The specific gravity was between 1020 and 1022; the amount of albumin from 0.5 per cent. to 0.9 per cent. In the sediment were many hyaline, granular, and fatty casts.

The abdomen was tapped on October 21, and 5 quarts 6 ounces of chylous fluid withdrawn; specific gravity, 1009. In the sediment, lymphocytes, 37 per cent.; epithelial cells, 63 per cent.

The boy left the hospital on November 2, 1908, in very poor condition, and remained so until February, 1909, when, after

tapping, his abdomen did not refill, and this improved condition persisted for three months. Since then he has had to be tapped every two weeks, fifteen times in all, up to September 27. (An average accumulation of about 12 ounces a day.)

His condition in September, 1909, was in all respects essentially the same as it had been a year before, except that the heart was 1.5 cm. farther to the left. He was tapped on the 28th and 5 quarts (5800 c.c) of opalescent fluid removed; specific gravity, 1006. After this the fluid reaccumulated very slowly, and he was allowed to go home on October 9.

CASE V.—*Alcoholic cirrhosis of the liver in a man, aged thirty-nine years; two and one-half months duration; omentopexy; no recurrence of ascites during the period of one year thereafter.*

A dentist, aged thirty-nine years, entered the hospital October 20, 1908. He had been in the habit of taking a pint and a half of whisky a day for the last two years, and an unknown amount for eight years previously. Two and one-half months ago he noticed that his trousers were tight around the waist. This increased so rapidly that four weeks later the abdomen had to be tapped, and 5 quarts of serous fluid were withdrawn. Since then he has been tapped four times, the amount being about the same each time. This means an accumulation of about 16 ounces a day. His feet have never been swollen, his appetite has been good, there has been no pain or other symptoms of any kind. The last tapping was a week ago.

Physical examination was essentially negative except for the evidences of ascites. The blood and urine showed nothing abnormal. Temperature, pulse, and respiration were normal. October 27, 14 pints 7 ounces of turbid yellow fluid were withdrawn. After tapping, the edge of the liver could not be felt below the ribs, but could be touched by reaching up behind the costal margin. The specific gravity of the fluid was 1008.

On October 28 the abdomen was opened, the liver found to be shrunken and irregularly nodular. Omentopexy was done, but by November 9 the patient had to be tapped again, and 9 pints of fluid were removed. (Rate of accumulation, 12 ounces a day.)

He left the hospital on November 22, 1908. November 29, 1909, the patient was seen and seemed to be in excellent condition. There was no return of fluid in the abdomen. The abdomen was tapped within a few days after his leaving the hospital in November, 1908, but tapping has not been required since. He now eats well, sleeps well, and looks well.

CASE VI.—*Ascites of very gradual onset, probably two years or more, in a non-alcoholic subject; no fever, no abdominal tenderness; positive tuberculin reaction; laparotomy shows no tuberculosis or cirrhosis; second operation done for cardiolysis; slight improvement thereafter; the ascites fairly controlled by energetic administration of cathartics and diuretics.*

A salesman, aged thirty-four years, entered the hospital November 13, 1908. His family history and past history not remarkable, habits good. For four or five years he has been gaining weight and has noticed that his trousers were tight about the waist. His usual weight is 150 pounds, now 158. The increase of his girth has been especially marked in the last year, and has been accompanied by dyspnea on exertion. During the last ten months his appetite has also failed; he has had a good deal of vomiting soon after meals, also troublesome constipation. He worked until nine months ago. Eight months ago he was tapped, and $6\frac{1}{2}$ quarts of clear fluid removed. After a month he began to refill. He has been treated during the last four months in the Out-patient Department.

Physical Examination. The heart's impulse extended 2 cm. outside the nipple line in the fifth space. The heart sounds were clear and there was nothing else of interest in the cardiac condition. The position of the apex shifted outward 2.5 cm. when he lay on the left side. The peripheral arteries were normal, and the lungs negative. The abdomen showed all the evidences of free fluid, and the edge of the liver could be felt 7 cm. below the costal margin in the mammary line.

He was tapped November 20; 202 ounces of yellow turbid fluid removed; specific gravity, 1020. In the sediment 85 per cent. of small lymphocytes, 15 per cent. of large lymphocytes. Nothing more felt after tapping. After an injection of 0.005 tuberculin subcutaneously there was a positive temperature reaction. The x-rays showed no evidences of tuberculosis in the lungs. At this time the spleen was easily palpable when the patient lay upon his right side, and it was noticed that there was a systolic retraction of the apical and precordial region. Adherent pericardium, tuberculous peritonitis, and cirrhosis were considered, but laparotomy December 5 showed no tuberculosis, and no evidence of disease in the liver so far as the surgeon's hand could discover. Dr. M. H. Richardson and Dr. Hugh Cabot considered the case to be probably one of pericarditis with adhesions and secondary ascites.

After that he got along until January 9, 1909, with two tappings, but was then operated on again, January 10, for the relief of adherent pericardium. Parts of the third, fourth, and fifth ribs were resected from their sternal attachments to a point 4 inches to the left. This seemed to allow the free retraction of the heart, and was deemed sufficient.

He returned to the medical wards on January 26, 1909, and under calomel diuresis the urine rose to 68 ounces and the amount of ascites was considerably decreased. This calomel diuresis was repeated ten days later, with success as before. On March 4 he was tapped, but only 4 quarts removed. The liver edge was then felt 5 cm. below the ribs. The specific gravity of the ascitic fluid was 1017. March 10 he was tapped again, but only 6 pints found.

A calomel diuresis was attempted on March 15, but was unsuccessful. It was evident that after the operation for cardiolysis the accumulation of ascites was slower, though this may have been due to the persistent administration of diuretics and cathartics. He was last seen March 27, 1909.

CASE VII.—A Russian Jewish millgirl, aged eighteen years, entered the hospital December 2, 1908, with a diagnosis of tuberculous peritonitis made in the Out-patient Department by Dr. W. H. Smith (O. P. D., No. 118,422). Her family history and past history were uneventful. Menstruation began at twelve and has been regular until within the last year, when it has become more frequent, and lately has come every two weeks and lasted four days each time. For three months she has noticed enlargement of the abdomen, and thinks she has been losing weight. Within the last month she has had some abdominal pain, paroxysmal and griping. Her appetite has been good and there has been no cough or other symptoms. Pulse, temperature, and respiration were moderately and irregularly elevated. The urine showed nothing abnormal. In the blood were 17,900 leukocytes per cubic millimeter December 3; 16,800 leukocytes December 7.

Physical examination was negative except as relates to the abdomen, which was prominent, tense, flat on percussion throughout, symmetrical, and gave a fluid wave. Girth at the umbilicus, 86.5 cm. The edge of the liver was not felt. No edema.

Tuberculous peritonitis was considered, but the leukocytosis and the extreme tightness of the belly made the diagnosis doubtful.

December 4 the abdomen was tapped above the pubes and 96 ounces of muddy, thick, viscid, ropy, alkaline fluid obtained; gravity, 1025. The fluid resembled very thick maple syrup and formed a jelly-like mass after heating. When diluted there was no precipitate or clot obtained by heat or by the addition of acetic acid. Biuret reaction negative. The addition of alcohol produced a heavy, ropy, tenacious precipitate (psuedomucine and paramucine). This precipitate, when boiled with acid, broke up into two bodies, one of which reduced Fehling's while the other gave the Biuret reaction. In the sediment there was nothing distinctive. The fluid was obviously characteristic of the contents of an ovarian cyst. By laparotomy a large multilocular cyst of the right ovary was removed without incident.

CASE VIII.—A housewife, aged thirty-seven years, entered the hospital February 15, 1909. She had had a miscarriage seven and one-half years ago, purposely induced; one living child five years old. Two threatened miscarriages in the course of this pregnancy. The baby was anemic for the first three weeks, but otherwise has been well. The patient had diphtheria twelve years ago, and the throat was sore for six weeks at that time. Three years ago began to have pains in her lower legs, especially along the

shins. The pains came at night, were very severe, and prevented sleep. There were no enlarged veins or other noticeable changes, but the bones were sore to the touch. A year later some ulcers appeared; the last one healed three months ago. Four months ago she had severe pain in the occiput, worse at night, and at this time three lumps appeared on her head about one inch in diameter, sore to the touch. One of them still remains.

Since her last pregnancy has had trouble with her nose, causing difficulty with breathing. At this time also, about five years ago, her hair came out profusely for a time. Two or three years ago she noticed a tumor in her left hypochondrium, which caused no symptoms, but bothered her in putting on her corsets. Last October she was operated on for hemorrhoids, and at that time the doctor said that her spleen was enlarged.


















Two and one-half months ago the belly began to enlarge, and she has been tapped twice, six weeks ago and three weeks ago. On examination there were many pea-sized bilateral cervical glands. Chest was negative; blood pressure, 135 mm. The upper border of the liver showed on percussion a median elevation just above the nipple line. The edge of the spleen was felt 12 cm. below the ribs. There was evidence of free fluid in the abdomen, and the girth at the umbilicus was 109 cm. Considerable soft edema of the ankles, and dark brown scars over the ankles and shins. On the forehead near the hair line a slight periosteal thickening, and another higher up in the hair on the frontal bone. X-ray plates show specific changes in the tibiae. Under antisiphilitic treatment and diuretin the patient improved rapidly. The fluid diminished in amount, but on March 2, 6 quarts were withdrawn, after which the edge of the liver could be easily felt 2 cm. below the ribs in the nipple line. The ascitic fluid was 1009 in specific gravity and showed 90 per cent. of mononuclear cells, about one-half of them large and one-half small. She left the hospital March 6, 1909, and up to date, May 1, 1911, has remained well.

CASE IX.—A shoemaker, aged fifty-three years, entered the hospital November 12, 1908. Family history and past history not remarkable. Eight years ago lumps appeared in the left side of his neck, and have not changed since then until a year ago, when additional and larger lumps made their appearance near those previously felt. Also similar lumps in the axillae and groins. Nine months ago lumps were noticed in the abdomen. Three weeks ago the belly and legs began to swell, and a week ago he was tapped in the Out-patient Department and 2200 c.c. removed; specific gravity, 1011; sediment lymphocytic. Eighteen months ago he weighed 180 pounds, a month ago 160 pounds. A gland was removed in the Out-patient Department, and a diagnosis of lymphosarcoma made.

On physical examination there was a mass of glands, roughly 10 by 8 cm., in the left side of the neck, not adherent to the skin,

and fairly movable. Elsewhere in the neck, axillæ and groins there were glands from the size of a bean to that of a hickory nut. The right pupil slightly larger than the left. Heart's apex, 1.5 cm. outside the nipple line. Cardiac examination otherwise not significant; lungs negative. The abdomen showed evidences of free fluid and large irregular tumors. The spleen and liver not made out. On the posterior rectal wall a mass half the size of the fist, hard and nodular, was palpable.

He was tapped on November 25 and 82 ounces of brownish-red fluid obtained. On December 4, 86 ounces more were removed. Specific gravity, 1015; sediment mostly epithelial cells. December 8, 115 ounces more were withdrawn. December 20, only 12 ounces. December 24, 17 ounces more. December 28, x-rays showed shadow over the whole left side of the chest.

CARDIAC WEAKNESS		1397
RENAL DISEASE		665
HEPATIC CIRRHOSIS		325
PERITONEAL TUBERCULOSIS		263
INTESTINAL OBSTRUCTION		86
OVARIAN TUMORS		63
UTERINE FIBROMYOMA		55
INTESTINAL CANCER *		56
PERITONEAL CARCINOSIS		53
PERICARDIAL ADHESIONS		36
HEPATIC CANCER *		30
PERNICIOUS ANEMIA		15
LEUKEMIA		11
MESENTERIC THROMBOSIS		8
ABDOMINAL LYMPHOMA		5
VISCERAL SYPHILIS ☉		4
CAVAL & PORTAL THROMBOSIS		2

* WITH GLANDULAR METASTASES

☉ HEPATIC, SPLENIC, ETC.

CHART I.—Relative frequency of the common causes of ascites as observed at the Massachusetts General Hospital (1870 to 1910).

Under diuretin, started December 26, urine rose on the 30th to 62 ounces, and several times subsequently 60 to 80 ounces were obtained as the result of diuretin. He was tapped December 28, and 7 pints obtained. On January 3, 50 ounces; January 9, 6 pints; January 15, 106 ounces; January 19, 96 ounces. He left the hospital January 21, and died soon after at home.

SOLID TUMORS OF THE OVARY.

1. *Cancer of the Ovary.* Fifty-four cases are on record at the Massachusetts General Hospital between 1870 and 1910. In 6 of these there was no operation or autopsy. Of the remaining 48, there were 19 cases (40 per cent.) in which a considerable amount of ascites was found.

2. *Fibroma of the Ovary.* Twenty well-recorded cases are to be found in our records. In 10 of these (50 per cent.) ascites was well marked at the time of operation.

3. *Sarcoma of the Ovary.* Five cases, one with ascites.

CYSTIC TUMORS OF THE OVARY.

There were 391 cases operated upon at the Massachusetts General Hospital (1870 to 1910) for multilocular ovarian cyst. In 31 of these, or 7.9 per cent., ascites was well marked at the time of operation. In 8 of these 31 the fluid was bloody or chocolate colored. In 1 the amount of serum was measured at 17 quarts.

TABLE III.

Disease.	No. of cases.	Rate of ascitic accumulation. Ounces per day.
1. Cardiac weakness	2	36-54
2. Cirrhosis of the liver	16	20
3. Chronic nephritis	5	13
4. Solid tumors of ovary	2	12
5. Neoplasms of the abdominal organs and glands	4	11
6. Adherent pericardium (before cardiolysis)	2	11
Adherent pericardium (after cardiolysis)	1	2
7. Uterine fibroid	2	8-11
8. Tuberculous peritonitis	15	5-6

TABLE IV.—Percentage of Ascites Occurring in the Different Varieties of Ovarian Tumor.

Diagnosis.	No. of cases.	Ascites found at operation in
Ovarian fibroma	20	50 per cent.
Ovarian cancer	54	40 per cent.
Ovarian sarcoma	5	20 per cent.
Ovarian cystoma	391	7.9 per cent.

Among 14 cases operated upon for *parovarian cyst* no ascites was found in any.

UTERINE FIBROMYOMA.

Among 723 cases operated upon for fibroid of the uterus, 55 cases, or 7 per cent., showed ascites. This was of small amount in 18 cases (2.4 per cent.); of large amount in the remaining 37 (4.6 per cent.).

In 10 of the 55 cases the fluid was bloody; in 2 others it was purulent.

In Table IV the relation of ascites to the different varieties of ovarian tumor is demonstrated. All these cases were operated on. I think many persons will be surprised, as I was, to learn how frequent is the association of ascites with benign ovarian growths such as fibroma and multilocular cyst. I have no idea why a small ovarian fibroma without metastases should produce extensive ascites so frequently.

Why should a small percentage (7.9 per cent.) of cystic tumors produce ascites? One would expect to find it in all cases or in none.

SUMMARY AND CONCLUSIONS.

1. Among the possible causes of extensive ascites we must not lose sight of the small solid tumors of the ovary.

2. Pleural effusion may be produced by an extensive ascitic accumulation. This association may lead to a false diagnosis of pleural and peritoneal tuberculosis.

3. The cure of both pleural and peritoneal effusions may result from excising a benign ovarian tumor.

4. Among all causes of ascites, tuberculous peritonitis may sometimes be recognized by the greater slowness of its accumulation of fluid.

5. Intestinal obstruction ranks fifth and disease of the female genitals sixth among the causes of ascites, being surpassed only by cardiac disease, nephritis, cirrhosis, and tuberculous peritonitis.

6. Besides the causes just mentioned, abdominal neoplasms and adherent pericardium are the only factors of importance in the production of ascites.

INFANTILE HYPERTROPHIC STENOSIS OF THE PYLORUS, BASED UPON A PERSONAL EXPERIENCE. OF SEVEN OPERATED CASES.

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FROM the first publication of a case of infantile pyloric stenosis by an American physician, Hezekiah Beardsley, in 1778, to the time of the publication of the Danish physician Hirschsprung's 2 cases, in 1887, little or no attention had been given to this important

and somewhat frequent malady of infancy, but with each succeeding year reports of cases are now multiplying, till what was once considered a rare disease is now coming to be recognized as of frequent occurrence, and our profession generally is growing fairly well acquainted with the clinical phenomena connected with it.

Evidently, however, it is either not recognized as frequently as it should be, or a decided feeling against operation must exist, since in a city the size of Cleveland but 9 cases, so far as I am aware, have been operated upon during the last five years. It is almost useless to go into the statistical results of operations for infantile stenosis of the pylorus, since, notwithstanding the increasing number of operated cases, the average mortality remains in the neighborhood of 50 per cent. It is to be noted, however, that in the hands of those whose number of cases is large, the mortality is decreasing slightly, and this may be ascribed to two causes—first, though not in my estimation the more important, because of increasing familiarity with the details of the operation and improved technique; and second, and of great importance if true, because physicians have had their attention called to the matter until they are quicker to recognize the symptoms and to urge operation, so that occasionally an infant is brought for operation that is not nearly moribund at the time. The laity must always be an obstacle to early operation, for marasmus is a well-known condition, and the feeling that a proper diet will correct the trouble will often prevent their consenting to an interference early enough to be of any avail.

Because of these considerations, it seems to me that it is proper to present some of the facts pertaining to this interesting and important infantile anomaly. My observations rest upon a study of 7 cases operated upon by myself, of which 4 lived and 3 died.

First, as to the pathological anatomy. It might seem that the stomach would be greatly dilated as a result of the pyloric obstruction, and while such cases have been reported, it is not uniformly so. In none of my 7 cases was there extreme dilatation. Some cases have, on the other hand, been reported in which the stomach was contracted to approximately one-half of the normal size. It is conceivable that this is due to the persistent and easy vomiting which does not permit of the stomach becoming habitually over-distended, and it may be that the greatly exaggerated musculature of the pylorus, by its almost complete obstruction, causes the much weaker cardia to give way and allow of easy regurgitant vomiting.

The pylorus itself is enlarged for a distance of nearly an inch, is pale and glistening in appearance, and has the consistency and feels on palpation much like the cervix uteri; so hard, indeed, that it is often compared to a piece of cartilage. Macroscopically, on cross-section, there is an exaggerated muscularis with a mucosa thrown into folds which in some cases completely block egress

from the stomach into the duodenum. Microscopically, as shown in the accompanying drawings (Figs. 1 and 2), a cross-section of the pylorus shows the following changes: (1) Almost complete

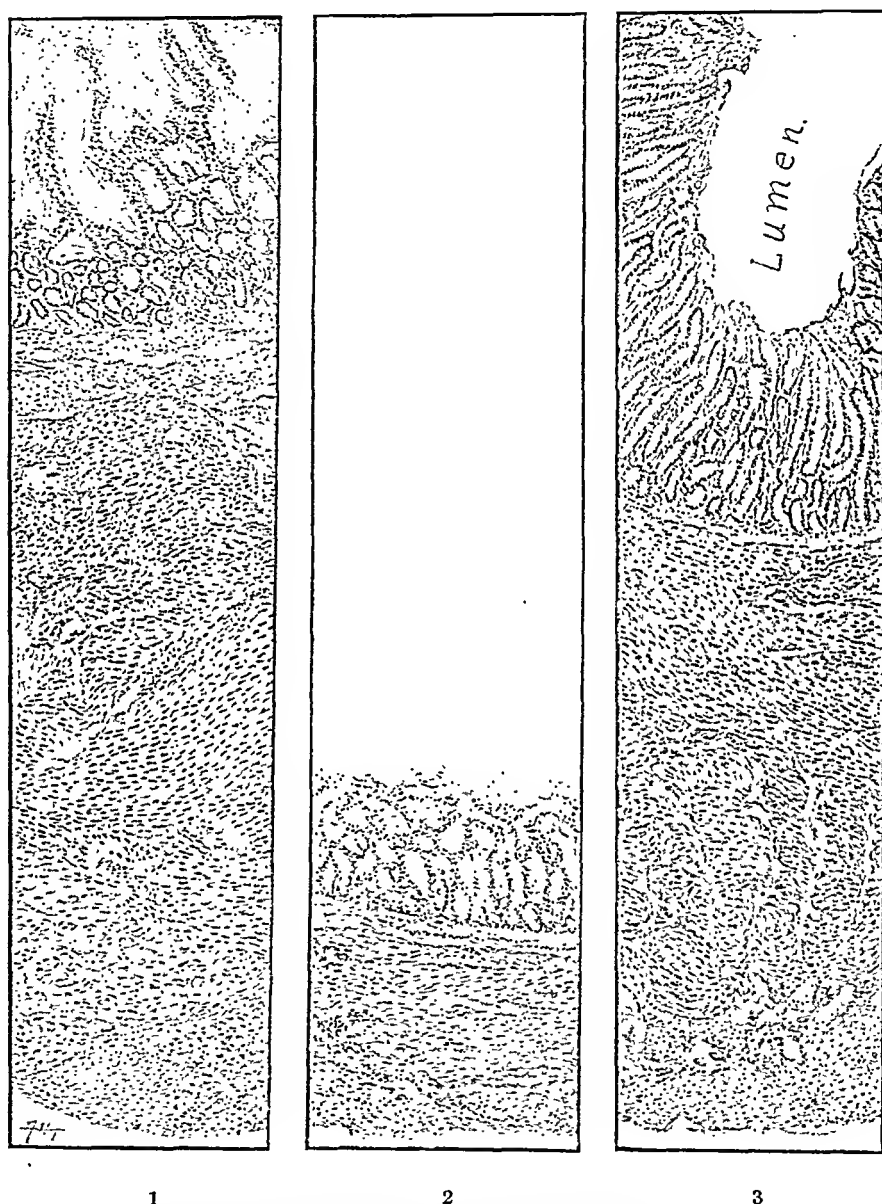


FIG. 1.—Microscopic sections of pylorus: 1, pyloric stenosis with no lumen; 2, normal pylorus; 3, pyloric stenosis in infancy with a lumen.

obliteration of the lumen, so that only a pin-point aperture exists. (2) The mucosa and submucosa are thrown into four folds by the contraction of the underlying muscle, and this seems to be the cause of the obliteration of the lumen. (3) There is a great thickening of

the circular muscle layer, and some fibrosis. (4) The other layers do not seem to be greatly changed, although some slight increase in the size of the longitudinal band of muscle is also to be noted, and a slight catarrhal inflammation of the mucosa. The muscular bundles in the submucosa do not appear to be increased.

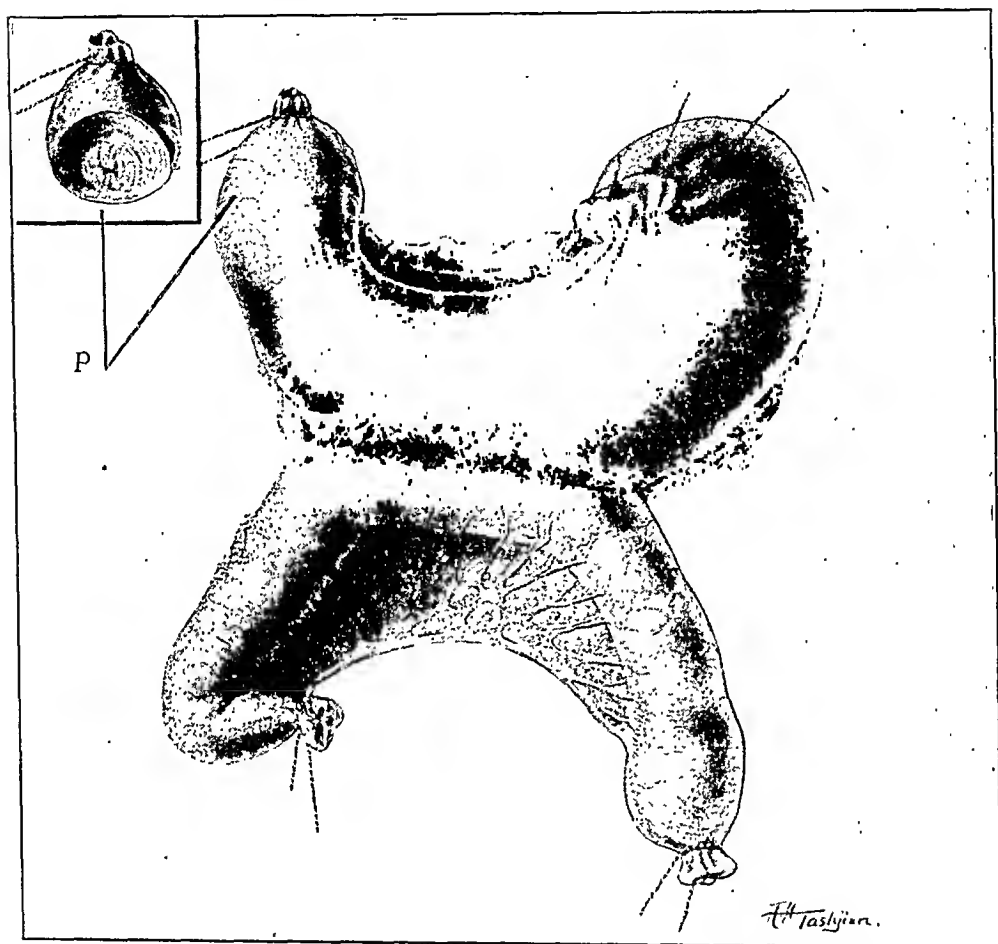


FIG. 2.—Pyloric stenosis in infancy with complete occlusion (p). This specimen was obtained from a patient on whom a gastro-enterostomy had been performed.

While the enlargement of the pylorus may, in its appearance and consistency, resemble a tumor, it is, as has been conclusively shown in numerous specimens, purely an hypertrophy, though in a rare case reported by Dent an aberrant portion of pancreas was found situated beneath the pyloric mucosa, and Torkel found situated beneath the submucosa an abnormal glandular structure which he considered to belong to a wandering Brunner's gland. Important contribution to our knowledge of the pathology of this condition has been made by Ibrahim and others by the examination of the stomachs of infants who had recovered under medical treatment from what had been clinically diagnosed as pyloric stenosis,

and died from other accidental causes. In these it was shown that the pyloric hypertrophy still remained, but that there had been developed a compensating hypertrophy of the stomach walls.

This observation has led Fredet and Guillemot to believe that in hypertrophic stenosis the organic lesion is not all, and that we must give a large place to secondary factors such as spasm, and to tumefaction of the mucous folds. On this basis it is easy to comprehend why and how the hypertrophic stenosis might not manifest itself until long after birth, and to answer the most serious objections to the theory of the malformation being of congenital origin. They also think that this explanation does away with the claim that hypertrophic stenosis cannot be cured by purely medical treatment, and that such reported cases of cure do not belong to the class of cases described by Hirschsprung.

While the evidence at hand at present is not sufficient to prove definitely that a true infantile as distinguished from a congenital hypertrophy of the pylorus does not exist, yet it seems probable that the latter hypothesis may well explain all the phenomena present.

The symptoms are of the greatest importance, for it is only by their early recognition and interpretation that we may expect to secure operative interference at a time when we may expect to lower materially the percentage of mortality. I believe that operative procedures have established their value as a life-saving measure. It remains now to secure the coöperation of the physicians and the laity in securing the operation at an early and favorable time. Naturally, the first symptom to attract attention is vomiting. This may not make its appearance for several weeks after birth or may begin with the first nursing. It seems to matter but little whether the child is breast fed or bottle fed, the cause is equally operative. At first the vomited matter represents but part of the ingested material, but eventually, notwithstanding every art of infant feeding, every mouthful of food is apparently ejected. Sometimes there will be a few hours or a day when the retention of a portion of the feeding will bring false hopes of recovery, to be followed, however, by the same distressing symptoms. In such cases we may imagine that the mucous folds of the pyloric outlet have become a little less congested, the opening a little less constricted, thus allowing a temporary escape of fluids. With the persistent vomiting we have a progressive emaciation of the infant, so that a child weighing eight or ten pounds at birth may weigh not over five or six pounds when it comes to operation some six weeks later.

If we can rule out the possibility of the vomiting being purely reflex from some other disease, it becomes of very great diagnostic importance. The absence or a small number of bowel movements soon becomes a marked symptom, and gradually the development of anuria is noted.

A symptom of the greatest importance, but one likely to be overlooked while the baby is fat and plump, is the dilatation of the stomach followed by a marked wave of contraction plainly visible as it travels toward the pylorus. In the greatly emaciated and delayed cases this phenomenon is peculiarly well marked, and may be watched as it arises spontaneously or may be brought into action by sharp palpation over the stomach. This ball-like tumor, with its peristaltic wave is so marked as to be readily made out by the nurse or mother.

It might be thought that the pyloric tumor would be readily palpable, but from my own experience such was not the case, for in only 2 out of 7 was I able positively to identify it. So that while its presence must be considered of the greatest significance, its absence in the presence of other confirmatory symptoms, is not to be seriously considered as evidence against the stenosis being present.

In their order, then, of importance, ruling out reflex disturbances, I would place the symptoms as: (1) Persistent vomiting, (2) emaciation, (3) visible dilatation of stomach, (4) visible peristalsis of stomach, (5) diminution and absence of stools, (6) anuria, (7) presence of palpable tumor of pylorus.

Colored powders incorporated in the food and absent from the stools might help in the diagnosis of pyloric obstruction, but I have not had an opportunity to make use of this method. In deciding for an operation one must take into consideration that the relatively early appearance of the symptoms mentioned speaks for organic rather than spasmodic stricture, and also that the latter condition should speedily respond to proper medical treatment.

The percentage of recoveries after operation has not been particularly gratifying (from 50 to 60 per cent.), if we consider it from the standpoint of percentage alone, but if we consider that these cases when they come to the surgeon have almost uniformly received long continued and varied medical care, and have reached the stage where it seems almost incredible that any of them should recover from gastro-enterostomy, then the percentage of recoveries does not seem unfavorable. They are emaciated, starving, and dying of thirst, and yet not only a severe operation must be gone through, but the extremely difficult problem of nourishment in the face of all these obstacles must be solved and solved quickly to save the infant.

The prognosis will improve as earlier diagnosis is made and earlier consent of parents to operation obtained. It would, I believe, be highly desirable to have a surgeon see suspected cases in consultation with the physician, not with a view to immediate operation, but in order better to arrive at an harmonious conclusion as to the safe and imperative time for surgical intervention. That even under the unfavorable existing obstacles to early operation improvement in the last three years has taken place, is shown by the results

in 38 such cases collected by Fredet and Guillemot, in which the mortality was but 26.31 per cent.

In my own series of 7 cases, 4 have recovered and are still living. In only 1 of these was the patient what might have been termed a fair operative risk. In only 1 of the 3 cases that died did I succeed in getting an autopsy. This was in an extremely feeble and emaciated child in which we had detected mesenteric tubercles at the time of operation. The child lived forty-eight hours, and died without any rise in temperature or other disturbances, probably from sheer exhaustion.

The drawings herewith presented are taken from this case and also from an apparently normal pylorus in a child ten days old dying from esophageal obstruction. One of the other deaths might possibly have been due to too severe crushing of the stomach or intestine with clamps (used in the first 2 operations) though of this I cannot, of course, be perfectly certain. The other lived eighteen hours, and died very suddenly after a convulsion and sharp rise in temperature.

My own conviction is that with even reasonably promising cases the mortality should be in the neighborhood of 25 per cent. but I do not believe that this reduction in mortality will be due very largely to an improved technique, but rather to securing patients at an earlier and more favorable time.

Regarding the technique, ether has been used in each case. It has been sought to retain the body heat by cotton wadding bandaged about the limbs and by warm water bags under the operating table pads. The incision has been slightly to the left of the median line, and has extended down to or below the navel, in one case enabling me to relieve an epigastric hernia at the same time. In some of the cases the stomach was previously washed out, but even then I found the stomach tensely distended with gas and a considerable amount of curds poured out when the stomach was opened. This distention of the stomach is quite annoying until the stomach has been opened.

Notwithstanding certain theoretical advantages in the posterior anastomosis, I have done the anterior operation in all the cases, making a long loop, but not doing an additional anastomosis between the two limbs of the jejunum. My reason for adhering to the anterior operation in these cases has been a fancied lessening of the shock due to the lessened exposure of the abdominal viscera, and to the somewhat increased ease of operation when the stomach is dilated and tense. Personally, while I now habitually perform the posterior no-loop gastro-enterostomy in adult patients, I have never been convinced that the results were in any way superior to those obtained by the anterior method, so that if the anterior operation offers any advantage either in facility or safety, it seems to me proper to make use of it.

The closure of the abdominal wound is of considerable importance, for in a number of reported cases the line of incision has given way under the severe and uncontrollable straining of a crying infant, and the intestines protruded through the opening. In hope of preventing this I have used the chromic catgut sutures for both muscles and peritoneum, and reënforced these by silk-worm-gut sutures through the entire thickness of the abdominal wall, removing part of them at the end of eight days and the remainder in ten to twelve days.

Feeding the child is of the very greatest importance, and I am much indebted to the physicians who have been associated with me in these cases for the valuable suggestions which have enabled me to formulate a general plan of attempt at nourishment that has proved fairly satisfactory. Sterilized water may be given, a teaspoonful at a time, as soon as the effects of the ether have passed off, and on the following day albumin water may be given in small amounts frequently repeated. For the first three days, however, most reliance must be placed upon rectal feeding, peptonized milk being used for this purpose at four-hour intervals. Whenever the mother's milk can be obtained, it should be used for this purpose. At the end of two to three days the stomach will be sufficiently quieted to permit of the addition of whey, and then mother's milk or modified milk in small quantities to the albumin water; and in exceptionally favorable cases the babe can be put to the breast to nurse for short periods.

No fear of leakage along the line of sutures need be felt if the operation has been thoroughly performed and the amount of nourishment given at any one time is small in quantity. The food is gradually increased as the condition of the child demands it, and the whole body rubbed with sweet oil from time to time to aid, however slightly, in the nourishment of the infant.

Dr. Scudder has made an elaborate and valuable study of the conditions following recovery, especially as to the metabolic changes, and, in a general way, these infants seem to do as well as others of the same age. The earliest of my own cases is now over four years old, and is as strong and hearty as any child could be expected to be. My third case is nearly three years old, and in perfect health. The fifth is one year old, and in excellent health. While the seventh and last is but seven weeks old, it has passed through the crisis of operation and feeding, and is gaining at the rate of about two ounces per day.

In concluding these fragmentary observations I beg again to call attention to the symptoms of the pyloric obstruction, and to the great importance of its early recognition, and appreciation that surgery offers a really brilliant prospect for its relief in properly selected cases.

LEUKEMIA IN CHILDHOOD.

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THREE cases of leukemia in young children have been observed by the writer within the space of two years. Their histories were as follows:

CASE I.—A girl, aged five years, living in Fresno, California, was brought to me in January 1909, referred by Dr. J. L. Maupin. Her past history was as follows: She had no illness of any kind until three years of age, when she passed through a protracted fever, six weeks in duration, diagnosed as malaria. In May, 1908, she was taken on a visit to Georgia, and there had mumps and chickenpox in light form; she recovered from these and returned to Fresno in June, but since that time she never seemed quite well.

Her present illness dated back to the Georgia trip, ever since which she had gradually grown paler, tired easily, and seemed breathless on exertion. But she never appeared seriously ill until an attack of tonsillitis two weeks previous to my seeing her, in which there was high fever and much swelling of the tonsils. From that time on she remained very weak and exhausted.

Physical examination showed the child to be very white, but well nourished. The lymphatic glands were moderately enlarged in both sides of the neck, both axillæ, and both groins. The spleen measured 10 cm. in area in the anterior axillary line, and the lower edge was distinctly palpable. The liver measured 12 cm. in the nipple line and its lower border was palpable half-way to the navel. The lungs were apparently normal. The heart showed a loud systolic murmur at all orifices, but the second sound was clear. The pulse rate was 140. A number of black and blue marks, the size of a bean, were visible over both shins and calves; and numerous smaller purpuric spots, petechial in character.

The urine was clear and showed no albumin or sugar. Blood examination, made on January 6, showed as follows: Hemoglobin, 21 per cent.; red corpuscles, 1,500,000, irregular in shape and size, poor in coloring, none nucleated, no malarial parasites; white corpuscles, 19,000; no polymorphonuclears; small lymphocytes, 96 per cent.; large lymphocytes, 4 per cent. On January 11 a second examination showed: Hemoglobin, 20 per cent.; red corpuscles, 1,150,000; white corpuscles, 14,000; small lymphocytes, 97 per cent.; large lymphocytes, 2 per cent.; polymorphonuclears, 1 per cent.; moderate poikilocytosis, polychromatophilia, numerous megalocytes.

Outcome. The child rapidly grew worse, with restlessness, drowsiness, delirium, refusal to eat; temperature, 101° to 103° by

rectum; pulse, 130 to 140; and died on the evening of January 11. The whole illness was apparently only six months at most in duration.

CASE II.—A boy, aged four years and five months, living at Santa Maria, Cal., was referred to me in June, 1909, by Dr. L. Bert Coblentz. The child had always been perfectly healthy before, never had had any of the diseases of childhood, or an illness of any kind. He had never been noticed to ail until about two weeks before I saw him, when he began to complain of pain in his left side, under the ribs. He also said he felt tired, and was not inclined to play. The pain, lassitude, and weariness gradually increased, and the boy grew pale, sallow, and breathless, so that he panted on slight exertion. The most noticeable feature had been his indisposition to play, and his weariness and lassitude; previously active and vivacious, he now cared only to lie down and rest.

Physical examination showed a boy well nourished, apparently well, tanned by the sun, bright and happy in manner. All superficial glands were found palpably enlarged, though none larger than a cherry, and all freely movable. The spleen was enlarged downward, with the notches plainly palpable along its lower edge, the free border extended to the level of the navel, and the total area of dulness measured 14 cm. The lungs and heart showed no abnormality, and the urine was clear. Over each arm and over the abdomen there were a number of small black-and-blue marks.

The blood showed: Hemoglobin, 45 per cent.; red corpuscles, 2,500,000; white corpuscles, 304,000; polymorphonuclears, 2 per cent.; large lymphocytes, 2 per cent.; small lymphocytes, 96 per cent.

This boy died on July 19, just six weeks from the time the first sign of his trouble was observed. His last two weeks were days of great distress from the splenic enlargement and pressure, with shortness of breath, nausea, constant moaning, apparently great pain, and finally delirium and coma.

CASE III.—A boy, aged seven years, living in Colusa, California, was referred to me in June, 1910, by Dr. C. A. Poage. The child was exceptionally well until two years of age, but he then had an illness diagnosed malaria, characterized by chills and fever, treated with quinine, and apparently cured. He had never seemed well since then, but had never had any definite attack of malaria, though he frequently had spells of fever, always disappearing in response to quinine. Three weeks before he was brought to me he had another attack of fever, seemed drowsy and weak, was supposed to have malaria again, and was given quinine. But this time his fever persisted, and he did not improve. Then it was discovered that his abdomen was enlarged. He had continued to be up and about, but tired easily, and had lost his appetite.

Physical Examination. On examination the child was found to be very pale, but fairly well nourished. The abdomen was distended

and protuberant, and showed many dilated veins. The spleen was greatly enlarged, occupying the left half of the abdomen, the lower border extended 5 cm. below the level of the navel, and the notches were distinctly palpable; but the right border did not pass the median line. The liver was likewise enlarged, measuring 12 cm. in its area of dulness, and its lower border being palpable 5 cm. below the costal margin. The lungs were clear throughout. The heart showed no evidence of disease except a loud systolic murmur over the pulmonic orifice. The pulse rate was 140, the temperature 100°. There was in this case nowhere any enlargement of superficial lymphatic glands.

The blood showed a hemoglobin percentage of only 15; the red corpuscles numbered 2,000,000, varied greatly in shape and size, were very pale, and a few nucleated reds were found; the white corpuscles numbered 480,000, of which the small lymphocytes were 96 per cent.; the polymorphonuclears, 3 per cent.; the eosinophiles, 1 per cent. This boy for a time apparently improved under treatment with iron, arsenic, and x-ray applications over the spleen and the long bones; the spleen reducing in size, the hemoglobin and red corpuscles increasing, while the white corpuscles decreased. But after that he rapidly relapsed, and death took place on September 16, about four months from the onset of the symptoms.

These cases, when analyzed, all resemble each other closely. No one would hesitate to diagnose them as leukemia. Probably every one would agree that they belong to the lymphatic type; and from the standpoint of duration all would be classed as acute. All took the usual course, uninfluenced to any extent by treatment, toward a fatal termination. The diagnosis means death and we know no way to avoid it. To any one who cares for his profession it is heart-breaking to meet with such cases, where there is not even a chance to save life; and no doubt others like the writer have asked themselves many questions about this disease, when they had the misfortune to meet it. There are several queries particularly that crowd upon one for answer.

1. What causes it? Age does not, for leukemia occurs in every decade of life. No part of the world escapes it, and no race of people. Is it due to an infection? Or is it a form of malignant disease? Or is it of any significance or only coincidence that two of the cases herewith reported had a malarial infection preceding their leukemia, as has happened also in cases reported by other observers? Not one of these questions can be positively answered; and a perusal of the large amount of literature written on this subject during the last few years will convince any reader that there is still no adequate explanation as to what causes leukemia.

2. What is the site of the disease? Is it the lymphatic glands, or the spleen, or the bone marrow, or all three? Here again there is a vast amount of contribution and of controversy, but no certainty.

There are two main theories propounded, each of which has numerous authorities behind it. One school of Germans arrives at the conviction that every leukemia, whether clinically it be lymphatic, splenic, or mixed in type, is due to disease of all the blood-forming tissues in every part of the body; though one tissue may be more advanced in its involvement, and so determine the clinical type. A second school believes that there are two distinct leukemias, a lymphatic due to disease of lymphatic tissues all over the body, and a myeloid due to disease of the bone-marrow. Those who are interested in this discussion should read an article by Naegeli,¹ in which he reviews and dissects 156 articles on leukemia that have appeared in current literature during the past decade, mainly in German literature. After finishing Naegeli's fifty pages of text, however, one feels but little enlightened as to the truth, no matter how interested by the argument.

3. Is leukemia a common disease in children? Fortunately we can answer this question in the negative. For a long time it was believed that it never occurred except in adult life. But gradually one case after another in childhood has been reported here and there by different observers. Still the total number is small, only about 50,² and the disease is, therefore, an uncommon one under ten years of age. When it occurs, the great majority of cases, like those herewith reported, are of the lymphatic type and run an acute course. All observers agree that the splenomedullary type is distinctly rare in childhood.

4. What can we do in the way of treatment? Absolutely nothing that holds out any hope of cure. Arsenic, x-ray applications, iron, transfusion, rest, oxygen, red bone marrow, all alike have failed. There is no known remedy that seems even to stay the course of the disease. Once the diagnosis is positive, the case is hopeless. Let us be thankful that such a diagnosis does not frequently have to be made.

MANAGEMENT OF FAILURE OF THE CIRCULATORY BALANCE IN CHRONIC INTERSTITIAL NEPHRITIS.

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FOR the purpose of laying a foundation for an intelligent consideration of the management of failure of the circulatory balance in chronic interstitial nephritis an introductory paragraph is desirable.

¹ *Ergebnisse der Inneren Medizin und Kinderheilkunde*, fünfter band, 1910, p. 222.

² Veeder, *Archives of Pediatrics*, January, 1911, p. 43.

The circulatory current begins with the secretion of the chyle into the intestinal lymphatics, continues through the thoracic duct, and enters the sanguineous system on the venous side near the heart, makes the lesser circuit, and is forced through the arteries and capillaries by the left ventricle. From the blood a requisite amount of nutritive material, in watery solution, is secreted through the capillary walls and enters the great extravascular circulation as tissue serum, and diffuses through the intercellular and larger serous spaces. In due course this liquid, contaminated by unused nutritive elements and waste matters, is secreted into the lymphatic radicles and conveyed through a system of ducts and purifying and filtration glands into the venous current. Portions of this liquid are also secreted into the venous ends of the capillaries and conveyed, with the surplus blood which passes the capillary barriers, through the veins to the right side of the heart. Other portions may be excreted by the kidneys, intestines, etc. The harmful materials, in aqueous solution, are directly or indirectly excreted mainly through the kidneys. The highly selective secretory and excretory functions of the specific cells of the lacteals, capillaries, lymphatics, kidneys, etc., are essentially vital, aided by the more measurable influences of composition, tension, pressure, velocity, etc., of the circulatory fluids and other physical and chemical factors. Although not demonstrable, nor indubitable, we may assume that the circulatory balance includes abundant direct and compensatory integrity and reserve capacity in circulatory fluids of adequate nutritive value, cardiac competency, vasomotor efficiency, transit-secretory activity, and other important factors.

In the cardiovascular-nephritic malady technically known as chronic interstitial nephritis there is found, in advanced cases, marked myocardial hypertrophy, arterial thickening, and renal fibrosis; the cardiac contractions are forcible, with increased resistance at the arterial terminals and great destruction of renal secretory tissue; the arterial circulation is energized, the venous flow is obstructed, and the tissue serum movement is retarded; the blood pressure is elevated, the proportion of venous blood is above the normal, and the tissue serum is largely increased in amount and altered in character. Under these circumstances the circulatory balance is deficient in reserve capacity, lacking in compensatory adaptability, delicately adjusted, and is comparatively easily broken. The loss of this balance may depend upon many factors, the majority of which are obscure or unknown. Although there may be other factors of equal or greater importance, with our present knowledge closest attention should be given to those which are obtrusively obvious, as myocardial weakness, especially that connected with insufficiency of the right auricular and ventricular aspiratory function; increased tenseness of peripheral obstruction; relative lymphatic incompetency; lessened areolar-tissue resiliency;

notable deviation from the normal composition of the tissue serum in many particulars, but especially in a diminution of the attraction, or adhesive viscosity of this liquid—in which the cells of the body may participate—by which the tissue serum is held in the intercellular spaces. It is probable that the most important of these, in the earlier stages, are venous stasis, lymphatic insufficiency, and cardiac suction failure.

Under these conditions of strain the circulatory balance is maintained partially, fitfully, and with difficulty; and often only by unconscious recourse to various devices for stimulating supplementary circulatory agencies, as, for example, a restless muscular activity, etc. In my experience manifest failure has usually followed some acute infectious malady.

Among the earliest readily recognizable signs of circulatory failure in these cases may be mentioned an increase in body weight, general plumpness, tenseness of all the tissues of the body, and an exaltation of the already high blood pressure. The face becomes fuller, and the trunk and extremities are symmetrically rounded out. Palpation reveals an increased sense of resistance, but there is no pitting upon pressure. Occult edema is present; manifest edema is imminent. The special subjective symptoms, although not robustly obtrusive, are nevertheless very significant. The physical activities of the patient are now curtailed; there is dyspnea upon unusual exertion; there is also sufficient dyspnea upon first assuming the recumbent posture to lead to the use of an additional pillow, and often this is supplemented by placing the arm under the pillows in order to further raise the head; he does not sleep as well as formerly, and occasionally he may be awakened by a severe attack of nocturnal dyspnea.

With progressive increase in the arteriocapillary obstruction and venous engorgement; with advancing myocardial weakness and dilatation; with an augmenting load of slowly moving tissue serum and lymphatic insufficiency; and after a period, which may be unexpectedly prolonged, during which there occurs a more or less urgent alignment of every primary reserve and supplementary force in an effort to sustain the toppling structure, the circulatory balance is definitely broken. The cardiac cavities are distended, probably with functional valvular insufficiency, and to the right auricular and ventricular aspiratory incompetency there is added the backward pressure of regurgitation. There is additional embarrassment in the venous circulation, especially in the liver, and dependent parts. Everywhere arteriosclerotic degenerative changes have become more marked, but especially is this true in the kidneys, where the widely spread atrophic changes in the arterioles and glomerular tufts and large increase of connective tissue produces the characteristic contracted kidney of this disease. Cellular destruction may account for the leakage of albumin into the urine.

The tenuous lymphatic radicles are compressed and, consequently and otherwise, relatively incompetent. The tissue serum is enormously increased in volume; it has become overburdened with toxic cellular wastes, and laden with an excess of salts; it is relatively, possibly absolutely, deficient in nutritive materials, and may have become notably acid in reaction; it has lost, markedly, in the quality of viscosity, and is not well held in the intercellular spaces, from whence it largely gravitates to the dependant parts, where it fills to distention the areolar tissue spaces and forms the characteristic dropsy of the "cardiac type."

The objective and subjective symptoms are prominent. There is a further increase in body weight. In the maintained upright posture the face, neck, and upper portions of the chest, parts which had been full and plump during the stage of occult edema, may be free from swelling; indeed, there may be here a noticeable deficiency of liquids. The lower limbs, genitalia, and other dependant parts are distended with dropsical fluids. In the edematous territory there is increased resistance offered to the palpating finger, and pitting follows pressure. The face and other regions from which the tissue serum has gravitated present more color than prevailed during the preceding stage, and they frequently show areas of brownish discoloration. In edema-free parts the muscles are flaccid, and there is usually absence of subcutaneous fats. As compared with earlier periods, the urine is less copious, of deeper color, of higher specific gravity, of increased acidity; it contains a larger proportion of salts, is more regularly and abundantly albuminous, and usually contains hyaline and granular casts. The blood pressure usually remains at its previous high levels. The patient is disabled. There is dyspnea upon slight exertion. He is unable to assume a horizontal position. With carefully adjusted supports he may be able to attain a more or less exaggerated semirecumbent posture; often this is impossible, and the tired sufferer obtains sleep only in various deviations from the upright position. He may be able to rest with the shoulders and head supported and inclined slightly backward. In some cases no pressure upon the back can be borne, and the patient sits erect, with or without inclination to one or the other side. In the most distressing cases he is compelled to lean forward with his head resting upon some supporting object. There may be Cheyne-Stokes respiration, frequently of slight degree; often it is typical; occasionally it is of the most distressing character. The pulse is increased in frequency and altered in character. Hemorrhages and other evidences of vascular degeneration occur. The natural course of these morbid processes is downward. Every phase of the circulatory embarrassment becomes more profound. The subjective symptoms increase in distressing features. Cerebral hemorrhage, or thrombosis, often occurs. Massive intestinal hemorrhages mark the exceptional case.

Toxemic coma or convulsions are not infrequent. Barring these and other somewhat accidental causes of death, the dropsical accumulation increases, rising higher and higher, and "when the water reaches the heart the patient dies."

Although rupture of the circulatory balance in this malady is not a common incident, nevertheless it should be considered as one of the possibilities sure to arise in a certain proportion of cases; indeed the likelihood of its appearance may be foretold with such fair assurance that the prediction may be verified by subsequent events. The recognition of the imminence, or actual presence of the lighter degrees of such failure is one of the fine arts of diagnosis; confirmed occult edema may be readily detected by any physician; the laity require no professional aid in the diagnosis of dependant dropsy.

How shall the cardiovascular-nephritic patient be protected from failure of the circulatory balance? Notwithstanding the paucity of etiological knowledge and the futility of attempts toward materially improving the pathological conditions, I am, nevertheless, of the opinion that earnest efforts along rational lines should be made toward conserving the patient's existing status, and, if possible, increasing his circulatory capacity. Not only this, but the conclusions which may be deduced from my observations are erroneous if the results of such well-directed measures are not generally beneficent.

The basic plan which I employ is, briefly, as follows: At intervals the patient is examined in such detail as to give such information as may be required concerning his environment and habits; nutritional requirements and supply; excretory capabilities and output; circulatory burden and reserve capacity. Upon the facts disclosed is based the advice given.

It is well to inform the patient that he has chronic interstitial nephritis, a malady in which the cardiac, vascular, and extra-vascular circulatory systems also participate fundamentally; that the disease is incurable, and the damages done are irreparable; that it is accompanied by inherent extra risks and dangers, and necessitates certain closely drawn restrictions; that, within limited bounds and probabilities, it is not incompatible with comfort, activity, usefulness, and possible long life.

The prescribed directions for diet, regimen, and medication should be based upon the requirements for the individual, as determined by the full examinations mentioned as preliminary to any advice. The diet should meet the caloric and other nutritional requirements of the patient; should consist of available foods and should be definitely formulated in terms comprehensible to the individual. The following is an example:

DIET. Breakfast. Take large helpings of bulky fruits, such as apples, pears, peaches, plums, prunes, cherries, strawberries, grape

fruit, bananas, melons, etc. Take an egg and two thin slices of bacon. Take an ordinary slice of bread, or an equivalent of toast, muffin, biscuit, wheat cakes, waffles, cereal, etc. Take tea, cocoa, coffee, milk, water, or carbonated water.

Luncheon. Take a very large helping of some vegetable salad, such as lettuce, tomato, asparagus, endive, etc., with a palatable dressing. There may be added pickles, olives, or other similar relish. Take a moderate amount of cheese. Take breads and liquids as at breakfast.

Dinner. Take vegetable, milk, or cream soups in variety. Take a piece of meat, fowl, fish, or game, about 2 by 2 by $\frac{1}{2}$ inch in size. Take moderately of gravies. Take very freely of all kinds of succulent vegetables, as asparagus, spinach, carrots, turnips, parsnips, pease, string and Lima beans, beets, beet-tops, onions, corn, tomatoes, celery, squash, marrows, cauliflower, cabbage, Brussels sprouts, mushrooms, etc. Take moderately of potato, sweet potato, rice, and other starchy foods. Take breads and liquids as at breakfast. Take moderately or sparingly of simple desserts.

Notes. The total amount of food taken should be the smallest which will maintain nutrition at the highest level. For your purpose the best measure of this will be the maintenance of your present weight, and a sense of well being. Should there be a tendency to take on weight the quantities of bread, potato, and other starchy foods should be reduced; should the body weight decline, these foods should be taken more freely. To be sure, if, at the beginning, there should be over- or under-weight, these departures from a desirable weight should be corrected by under- or over-nutrition, continued until a satisfactory standard has been attained. As a rule, apples, peaches, pears, and similar fruits should be cooked. Succulent vegetables should be properly cooked, as should all foods requiring this process. At luncheon there may be substituted for the salad fruits, as at breakfast, or succulent vegetables, as at dinner. Under circumstances to be specifically defined from time to time, milk and cheese should be taken regularly at every meal. Upon rising, and also two and one-half or three hours after meals, take a small glass of water, or of carbonated water. There should be taken a total of from 3 to $3\frac{1}{2}$ pints of liquids of all kinds during the twenty-four hours, unless specifically advised to the contrary. Avoid alcohol, foods which are notoriously difficult of digestion, and all foods which disagree.

REGIMEN. Take such a fair amount of active physical exercise as shall be specifically directed from time to time. Massage should replace active exercise should the latter be impracticable. Avoid as far as practicable exposure to infectious diseases; should these maladies be contracted there should be prompt and close medical supervision. Avoid tobacco. Avoid all feats of strength and

endurance; all overexertion, strain, and undue exposure. The clothing should be comfortable. Comfortable bathing with regularity, or as to be specifically directed. The body weight should be taken weekly, and recorded. Once a week all the liquids taken should be measured, as well as all the urine voided, and record made of the same. Should the bowel movements be liquid an estimate should be made of the quantity and record made of the same. Specimens of the twenty-four hours' urine, measured and labeled, should be submitted for examination once a week, fortnight, or month, as specified. Directions to be given as to the methods by which the above shall be done. Should there occur headaches, disturbances of vision, difficulties of breathing, nocturnal dyspnea, the requirement for more than one pillow in sleeping, rapid increase in weight, swelling of the feet, or any other event which is out of the ordinary, or which is not understood, consult your physician at once. Submit yourself, at the regularly appointed times, for full examination.

MEDICINAL. Once in four weeks, or as directed, take two freshly made pills of mercurial mass, of 5 grains each, every night for three days, followed the first time by half an ounce of castor oil in the morning, and the other two mornings by a saline cathartic. Other medication to be specifically directed.

Immediately upon the detection of the slightest evidences of circulatory embarrassment or occult edema, or of manifest dropsy or uremia, the patient should be given active and efficient treatment. He should be put to bed, in as nearly a horizontal position as possible, where he should remain until the circulatory balance has been restored. This I consider the most important medical measure which can be instituted, under the circumstances described, in these cases. The venous system is thus given an opportunity to drain itself easily; and the heart to regain its tone, largely because of the lessened strain upon its right-side aspiratory action, and the relief given to the ventricular contractions. In various ways probably every part of the circulatory system is offered more or less positive relief. It is usually advisable to prescribe efficient doses of an active preparation of digitalis, as, for example, the freshly prepared infusion of the best English leaves of the current year, properly gathered and preserved. At this time there should be no hesitation upon theoretical grounds pertaining to the exalted blood pressure; the bald fact remaining that it is not materially raised by this drug, in these cases under the circumstances mentioned. More or less vigorous massage is useful, probably by increasing the venous, lymphatic, and tissue-serum movement.

Already the composition of the tissue-serum is notably altered. It is especially significant that it contains an excess of sodium chloride; is usually acid to phenolphthalein; and is deficient in viscosity. If nutritive elements are present in normal amounts

they are probably less available than in health, or the cells do not so readily appropriate them, for, certain it is that at this time there is a measurable decline in nutrition, particularly apparent in loss of reserve fats. The possibility of improving the character of this liquid by appropriate feeding lends peculiar importance to the diet at this time. The presence of an excess of chlorides in the tissue serum, together with the well known effects of sodium chloride in increasing edema, has led to the formulating of the so-called "salt-free" diet. While approving of giving this subject the most careful and favorable consideration, I wish here to enter an emphatic protest against dignifying the important process of adjusting the amount of table salt to the requirements and capacity of the body tissues by exalting it as a system of treatment. With the object in view of replacing the excess of sodium chloride by the like salt of lime, and possibly increasing the viscosity of the tissue serum, I am accustomed to give lime, preferably in the form of the lactophosphate, in fairly large doses, and with apparent benefit. The same results may be had by giving, in suitable quantities, milk, gelatine, and other lime-bearing foods. To my mind the question of how to maintain the mutual attraction between the tissue cells and tissue serum, and the viscosity of the latter, in order that this liquid, as it envelops the cells of the body, may move along with just sufficient velocity to allow a maximum amount of required nutritional cellular absorption, and of waste extrusion, is one, if not the most important and urgent, of the problems confronting us.

Reverting to the details of the diet at this time, it is clear that, because of the loss of reserve fats, and the use of the body proteids, as evidenced by the increased urea excretion and loss of weight, particular attention should be directed toward meeting, fully, the caloric requirements of the individual, and the directions for this should be definitely formulated by the physician. Until every vestige of tissue serum excess has been drained away, the intake of liquids should be well below that of excretion, as determined by actual weight and measure. With restored circulatory equilibrium the ingested liquids should approximate the standard which experimental study has proved to be most suitable for the patient. It is well, at this time to repeat the mercurial mass at more frequent intervals, and the saline may be given every morning, if the exigencies of the case requires. The rigidity of this plan of management may be lessened with precautionary oversight, but there should be a close adherence to the fundamental principles involved. These special measures should be continued for a sufficient time to allow as complete restoration of the circulatory balance as possible. This may be, in rare cases, about a month; usually at least six weeks are required; in some cases, especially those in which a recent infectious illness has been experienced, a much longer time will be necessary.

Between the stage of this malady which has been just considered and the terminal one is a wide gap and a long interval. During the intervening periods there will have been some in which the patient's condition is eminently satisfactory, the circumstances considered; others of relapses, disappointments, and distress. The management will have been one of increasing care and strictness, passing gradually through the steps intervening between those which have been mentioned and those which will now demand our attention.

In the stage to which I now refer the patient has passed through a prolonged period of great distress. There has been such respiratory distress as to prevent the patient assuming the recumbent posture, sleeping fitfully in his chair in a more or less erect and uncomfortable position. There have been a variety of uremic manifestations, such as headaches, wakefulness, muscular twitchings, visual scintillations, drowsiness, mental dullness and aberrations, etc. Retinal and other hemorrhages may have occurred. Occult edema has appeared, and gradually increased, with augmented distress, to the greatest tension, when, fitfully, the restraining barriers of intercellular tissue-serum attraction and areolar tissue resiliency gives way, and with notable relief from the distressing symptoms, dependent dropsy is an established fact. The patient is now in a present and visible danger; the management assumes an importance, not greater, but more acute. What shall it be?

Removal of the superfluous tissue serum is an essential first step. This is best accomplished by the use of elaterin. The method of procedure is important. During three days the diet should consist of thin gruels, cream and water soups, tea, coffee, water, and carbonated waters. The first and second days the total quantity should be about 1500 c.c. per day; during the third day the quantity should not exceed 1000 c.c., and the gruels and soups should be taken very sparingly or omitted. Every night, including the night preceding the first day, there should be taken 10 grains of mercurial mass, in two freshly-made pills of 5 grains each. The first following morning there should be taken an ounce of castor oil; on each of the other mornings there should be taken an efficient saline cathartic. Beginning with the fourth morning, give $\frac{1}{20}$ grain pure elaterin every hour for three doses; later $\frac{1}{10}$ grain every two hours until ten or twelve very free watery movements have been secured. This may require two or three days, during which time the patient should have no solid foods, and very little liquids. Later the standard diet, modified as may be required, should be gradually resumed. The total number of liquid stools will probably be from 15 to 20, and the quantity of tissue serum drained away, from 5 to 20 pounds. The filtered serum thus evacuated should be analyzed, and the results recorded. It is usually acid, straw or

amber colored, having a specific gravity of from 1005 to 1030, and heavily laden with chlorides. The odor is sometimes peculiarly offensive. Following the intestinal drain the flow of urine usually becomes very free; I have seen the day's excretion reach the enormous quantity of 6000 c.c., when previously it had been scanty. The siphonage thus started ordinarily continues as a free flow until the edema has completely disappeared; nevertheless, this action should be assiduously encouraged and stimulated, for example, by the use of infusion of active digitalis leaves, theocine, external warmth, the recumbent position, etc. During the entire course the intake of liquids should be well below the output. The advantages of this method of removing dropsical liquids lies, primarily, in the fact that they are selectively excreted by the intestinal and renal cells, ordinarily the albuminous and other useful nutritive materials largely remaining behind.

In some cases, from various causes, the method thus shortly outlined is impracticable. It will then be necessary to remove the serum directly from the subcutaneous tissues, preferably by means of Southey's tubes. The pointed stylet makes an opening through the skin mainly by spreading the tissues; the small tubes are tightly grasped by the elastic tissues, thus preventing leakage; closure promptly follows removal of the tubes, and with the employment of full antiseptic precautions, infection is almost unknown. Two tubes in each leg, one inside and the other outside, inserted just above the ankle, or at any other more available points, are usually sufficient. Rubber tubes of the smallest caliber, as soft rubber catheters, should be attached to the ferruled ends of the silver tubes and tied with ligatures, the ends of which may be used in retaining the tubes in place. In this manner the surface is kept dry, the draining tissue-serum being conveyed to suitable receptacles, thereby adding to the comfort of the patient and reducing to a minimum the liability of infection. The patient should assume a semirecumbent posture, preferably sitting in a chair, or lying in a specially prepared bed which insures an inclined plane for the body, with the feet in the most dependent portion. He should be made as comfortable as possible, inasmuch as much fortitude is required. The drainage should be continued until the edema has largely disappeared, and the flow reduced to an insignificant amount. Usually there may be removed in this manner from 10 to 30 pints in twenty-four hours, and from four to seven days of gradually decreasing flow will be required to complete the process. The advantages of this method lie in the directness of the attack and the certainty of results; the very obvious objection to it is that the tissue serum is drained off as a whole, including its albumin and other nutritive materials. Upon removal of the tubes a dry antiseptic powder should be used and an elastic bandage applied to the

feet and legs. The feet should be kept at a higher level than the hips. The small openings rapidly close under this management.

Removal of these large dropsical accumulations discloses an astounding degree of emaciation, although this may be anticipated with great exactitude from the moment when occult edema is detected. With complete exhaustion of the stored-up fats, and the patient's proteid tissues already heavily drawn upon, we are brought face to face with a very formidable situation, inasmuch as the continuation of this condition will lead to starvation acidosis, with all its distressing features. To meet this condition there will be required a most careful adjustment of the dietary, in the formulating of which close attention should be given to its every detail. The following may be considered as typical only, inasmuch as the individuality of the patient and his requirements must dictate the dietary:

	Grams.	Calories.
Breads of all kinds, a minimum of	124.0	496
Oatmeal, or other cereal, a minimum of	31.0	124
Rice, variously prepared, a minimum of	31.0	124
Potato, variously prepared a minimum of	62.0	248
Meat, fowl, or fish, lean, a minimum of	31.0	124
Meat, fat, a minimum of	31.0	279
Eggs, a minimum of	96.0	384
Sugar, a minimum of	15.5	139
Butter, a minimum of	15.5	155
Cream, 15 per cent., a minimum of	124.0	186
Milk, 3 per cent. cream, a minimum of	500.0	150
Cheese, a minimum of	15.5	162
Total		2571

To these there may be added, or to an equitable extent substituted for a portion, all kinds of succulent vegetables and fruits, properly prepared. The table salt should be limited to somewhat less than the secretory capacity of the patient's kidneys. The same should apply to the liquids taken; ordinarily from 1000 c.c. to 1500 c.c. is the proper quantity, but it should not exceed the output by the kidneys and intestines.

In conclusion, it is clearly impracticable to follow the various lines of management which should be pursued through the advancing stages to a fair or moderate symptomatic recovery; and quite impossible to do so through the deviousness of the downward path. Suffice it to say that some of the successes may well take rank among the marvels of medical achievement; and even in those, only too numerous, pursuing an unfavorable course, we may not infrequently feel assured that by giving our patients all the advantages of the methods and details of management which the present state of knowledge permits, with the measure of perception, tact, diligence, and fertility of resource which should be given them, their days have been lengthened and made more comfortable and useful.

**BACILLUS DYSENTERIÆ RECOVERED FROM THE PERIPHERAL
BLOOD AND STOOLS OF CASES IN PANAMA.**

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THE following cases are reported for several reasons: (1) To note the occurrence of *Bacillus dysenteriae* in this region, the Canal Zone and the native village of La Chorrera, Republic of Panama. (2) The isolation of *Bacillus dysenteriae* (Shiga strain) from the circulating blood in a fatal case of dysentery. (3) To emphasize the value of special media (Endo) in shortening the otherwise laborious technique of isolating *Bacillus dysenteriae* from stools.

In their efforts to isolate the dysentery bacillus from stools and autopsy material many workers inoculate large numbers of agar plates from broth cultures and then endeavor to pick the desired colonies after a macroscopic and microscopic examination. The suspicious colonics are then usually inoculated into a nutrient medium containing glucose and litmus, all gas formers being rejected, the rest saved for further study. Sometimes the number of colonies thus studied runs into the hundreds. This entails many hours of work, which work may be done in almost as many minutes by the use of a differential medium at the start. Many differential media have been suggested and used¹ for the isolation of the typhoid bacillus, but little advantage seems to have been taken of this method in isolating the *Bacillus dysenteriae*.

In our routine work of examining the stools and urine of typhoid convalescents for typhoid and paratyphoid bacilli we have used Endo's² medium, and on account of the several biological characteristics which the dysentery bacillus has in common with the typhoid bacillus, this medium immediately suggested itself to us as an excellent one for the isolation of the dysentery bacillus.³ Neither the typhoid nor the dysentery bacillus ferments lactose, while many of the intestinal bacteria, especially *Bacillus coli* and its near relatives, as well as many representatives of the coccaceæ, ferment lactose.

In Endo's medium 10 grams of lactose and 1.8 c.c. of a 10 per cent. alcoholic solution of basic fuchsin are added to the liter and

¹ Pratt, Boston Med. and Surg. Jour., 1907, clvi, 744, 788, 813.

² Centralbl. f. Bakt, 1904, xxxv, 109.

³ Proceedings Canal Zone Medical Association, August, 1909.

the medium then barely decolorized by the addition of a 10 per cent. aqueous solution of sodium sulphite.

According to Endo,⁴ fuchsin apparently is composed of the acid salt rosanilin $C_{20}H_{19}N_3HCl$. Rosanilin is a colorless so-called leucobase which, with various acids, such as lactic acid, acid salts, etc., forms a red dye. The acid component of the red rosanilin salt is easily reduced by sodium sulphite. The decolorized rosanilin combines with the acid produced by the colon bacilli and regains its red color.

This gives a red color to a colony which splits lactose with the formation of acid. In sharp contrast with the red *Bacillus coli* colonies, the typhoid, paratyphoid, and dysentery colonies which do not act on the lactose come out small, colorless, and translucent, like small drops of dew. The length of the period of incubation varies from twelve to forty-eight hours, according to the nicety of adjustment of the reduction with the sodium sulphite. There are several other microorganisms which present a similar appearance on this medium, as, for instance, *Pseudomonas pyocyanea* or the paracolon bacillus, but their number is usually so small that they do not interfere seriously with this method.

In our routine work all suspicious colonies are inoculated into broth; this is incubated for twenty-four hours, and then subinoculations are made on agar slant, potato, in litmus milk, Dunham's, and into each of the following semisolid media: Glucose, lactose, dulcete, saccharose, maltose, mannite, dextrin, and galactose. The semisolid medium is used on account of its greater sensitiveness in exhibiting gas formation and motility. Agglutination tests are made with a saline emulsion of the growth from the agar slant and *Bacillus dysenteriae* immune serum.

With the use of the Endo plates the examination of a large number of *Bacillus coli*-like colonies is also obviated, as the original material is immediately spread on the plates without the previous inoculation of broth. When broth is inoculated, *Bacillus coli* multiplies much more rapidly than *Bacillus dysenteriae* and increases the difficulty of detecting and isolating the latter.

The first patient from whose stool we isolated *Bacillus dysenteriae* was a white American working in the laboratory. The source of infection is doubtful, for the patient lived at Ancon, where there has been no epidemic gastro-intestinal disease since "El Mayo"⁵ in 1905. He may have become infected from an autopsy held on July 29, 1909, a few days before the onset of his attack.

The autopsy was one of chronic nephritis with ulcerative colitis. Cultures from the gut, however, contained chiefly *Bacillus coli* and

⁴ Loc cit.

⁵ "El Mayo" is the local name for an epidemic diarrheal disease which appears in Panama at the beginning of the rainy season.

streptococci. No *Bacillus dysenteriae* could be detected. Another possible source of infection was one of enterocolitis in an American child, aged two years, born in the United States. The child had been embalmed by the patient whose case is reported here, and opportunities for infection occurred June 23 and June 29, four to five weeks before the onset of the disease in question.

He was sick one day before admission to the ward. The second day in the ward he had fifteen movements, the third day forty, and from then on a gradually decreasing number. These movements were fluid and contained much mucus, pus, and blood. He ran a slight continued fever, the highest point reached being 100° F. On the seventh day of his illness a specimen of his stool was sent to the laboratory. This was streaked on Endo plates, and the resulting growth showed many typhoid-like colonies. Fifteen of these were planted in glucose semisolid. Some of them were *Pseudomonas pyocyanea* but three colonies on subcultivation in thirteen media had the cultural characteristics of *Bacillus dysenteriae*. These three colonies were all agglutinated with the "Y" immune serum in a dilution of one to six hundred in less than two hours, and by the Flexner and the Shiga immune sera in lower dilutions. This was a severe and typical case of bacillary dysentery due to the "Y" bacillus and apparently was a sporadic case.

The second case is one which has several peculiar features. The patient, a negro and Zone charity case, entered the hospital on May 13, 1910. He had been sick for six days when he entered the hospital and gave a history of abdominal pain and of passing blood and mucus. The physical examination showed marked tenderness over the colon, few rales in the lungs, enlarged glands, heavily coated tongue, weak heart sounds, slight injection of the conjunctivæ, enlarged liver and spleen. He had a leukocyte count of 27,500. All his movements were fluid, containing much blood and pus. On the first, fourth, and fifth days after admission he had severe hemorrhages from the bowels. The largest number of bowel movements recorded on any one day was eleven. The highest point his temperature reached was 101° F. On the night of his admission he had a severe hemorrhage from the bowel, and a blood culture was taken the following morning. On account of this loss of blood, only a small amount was taken (about 4 c.c.), and this was inoculated in bile-glycerin-peptone solution, not being inoculated in oxalated broth as is usually done. This bile-glycerin-peptone was incubated for twenty-four hours and then agar plates made. At the end of twenty-four hours' incubation these showed many colonies which were smaller and more transparent than typhoid colonies. Agglutination tests were made with these and typhoid immune serum, paratyphoid A, immune serum, paratyphoid B immune serum in various dilutions. In none of these did agglutination occur.

Several colonies were now taken from the agar plates and grown in broth for twenty-four hours and these subinoculated on agar slant, potato, in litmus milk, in Dunham's medium, and into each of the following semisolid media: Glucose, lactose, dulcitol, saccharose, maltose, mannitol, dextrin, and galactose. On these media each culture showed the cultural characteristics of *Bacillus dysenteriae* (Shiga strain) with the exception that the litmus milk did not become alkaline after prolonged incubation. Agglutination tests were carried out with some fresh therapeutic antidysenteric serum which we had just received from Mulford. This serum is a combination of two sera, Shiga and Flexner. Each component will agglutinate the dysentery bacillus from which it was derived in dilutions of one to one thousand, and other varieties in a dilution of one to five hundred. Testing our organism with this serum, it agglutinated in dilutions of one to one thousand and lower in less than two hours, and in a dilution of one to two thousand in two hours. As a matter of control, agglutination tests were carried out with this serum and typhoid, paratyphoid A, paratyphoid B, the colon bacillus, and several other organisms of this group, in every instance with negative results.

The patient died on the tenth day of the disease. The autopsy was performed by Dr. H. C. Clark. From the autopsy findings the following is quoted: "Very slight increase in peritoneal fluid. All mesenteric, mesocolic, and periportal glands are noticeably enlarged, the ones about the cecum showing the greatest change. No visible change in the peritoneal covering of the intestines. . . . When the large bowel was opened there was found to be a very diffuse diphtheritic inflammatory process from the rectum to the ileocecal valve. In the cecum and ascending colon it had become almost gangrenous, while throughout the rest of the gut a bright red, coarsely granular, inflammatory process with a diphtheritic exudate was found."

Hence we have a case of acute dysentery authenticated by autopsy findings in which the dysentery bacillus was recovered from the blood stream four days before death, proving that *Bacillus dysenteriae* may be found in the circulating blood in spite of statements to the contrary by several authorities.

The only detail in which this bacillus differs from the Shiga bacillus of classical description is in its effect upon ordinary litmus milk. It turns this a lilac color, which is a sign of slight acid reaction and remains thus permanently. Torrey⁶ states: "Several cultures belonging in Group I, which when first isolated were entirely typical in the effect on litmus milk, did not produce, about six months later, a marked alkaline reaction. After returning to amphoteric there was no change to alkalinity, but, if anything, the

⁶ Jour. of Exper. Med., 1905, vii, 372.

medium appeared slightly more acid than the control after three weeks' incubation."

Again, our milk from the hospital dairy, although neutral to litmus, is almost invariably as strongly acid as may be used, requiring from 15 to 17 c.c. of decinormal sodium hydroxide per liter to neutralize it, using phenolphthalein as an indicator.

Jordan⁷ makes the positive statement that the dysentery bacillus is not found in the blood stream.

Castellani and Chalmers⁸ state that the dysentery bacillus has been recovered from the blood stream by Rosenthal and Markwald, but give no reference.

The third case was that of an infant, aged eight months, seen during an investigation of a reported outbreak of diarrheal disease at the native village of La Chorrera, August 22, 1910, about twenty-five miles from Panama. The parents gave a history of the child having dysentery. A Löffler blood serum slant was inoculated with swab material from the rectum. Two days later, when the culture reached the laboratory, a saline emulsion of the growth on this slant was made and spread on Endo plates. From these plates several organisms were recovered which conformed culturally with the "Y" organism of Hiss and Russell. These agglutinated with Mulford's anti-dysenteric serum in a dilution of one to one thousand in one-half hour.

To summarize: (1) By the use of a differential medium (Endo's) we have been able to isolate *Bacillus dysenteriae*, the "Y" type, from two sporadic cases of dysentery, one a white American, an inhabitant of Ancon, Canal Zone, the other an infant living in and native of the small village of La Chorrera in the Republic of Panama.

2. We have recovered from the circulating blood of a fatal case of dysentery, in our routine blood culture work, *Bacillus dysenteriae*, one which agglutinates with antidysenteric serum in a dilution of one to two thousand and is culturally of the Shiga type.

NOTE ON THE FAVORABLE INFLUENCE OF QUININE AND UREA HYDROCHLORIDE IN LARGE DOSES UNDER THE SKIN IN THE TREATMENT OF ACUTE PNEUMONIA, LOBAR AND LOBULAR.¹

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THERE is a long-standing tradition that quinine given early will abort an attack of lobar pneumonia. In an early experience

⁷ General Bacteriology, p. 285.

⁸ Manual of Tropical Med., 1910, New York.

¹ Read before the Association of American Physicians at Atlantic City, May, 1911.

of the writer's, 60 grains of quinine sulphate given in error in a period of five hours, beginning two hours after the initial chill, apparently acted in this manner. Galbraith's revival of the treatment of pneumonia by quinine in massive doses (1904) led the writer to employ it at the Philadelphia General Hospital and at the Hospital of the Jefferson Medical College; soon, however, substituting hypodermic for gastric administration (as advised by Aufrecht, Petzold, and Henry),² and choosing the most active salt of quinine, namely, the double hydrochloride of quinine and urea, with which he has had such favorable experience in the treatment of malaria.³ The initial dose (regulated somewhat by the height of the temperature) is 1 gram to 1.6 grams (15 to 25 grains). This is followed in three or four hours by a second injection, and perhaps by a third and even fourth injection, at some time within the first twenty-four hours, according to results. The same plan is pursued on the second day of treatment and on the third day, if necessary. Usually from 6 to 10 grams are given in from forty-eight to sixty hours. After that smaller doses (5 to 10 grains—0.3 to 0.6 gram daily) are sometimes continued by the mouth.

Cinchonism does not develop. Temperature and pulse-rate fall gradually and proportionately, and respiration more rapidly, with a tendency to restoration of the normal pulse-respiration ratio. Blood pressure may at first decline with temperature and pulse frequency, but soon returns to the former or a higher level; often it remains stationary or increases. The complete clinical picture, so far as regards the rational symptoms, objective and subjective, is thus favorably changed. The patient professes comfort; the pulse is full and strong, of moderate frequency and good tension; respiration is astonishingly easy, even when the rate is not markedly altered; the cough is greatly diminished; and delirium, if present, is abated, or may even cease. Crisis does not occur. Termination is by lysis at about the ordinary time, five to twelve days. The only critical phenomenon observed, and this but rarely and in slight degree, is perspiration. Usually there is some mild sweating with the early fall of temperature and respiration.

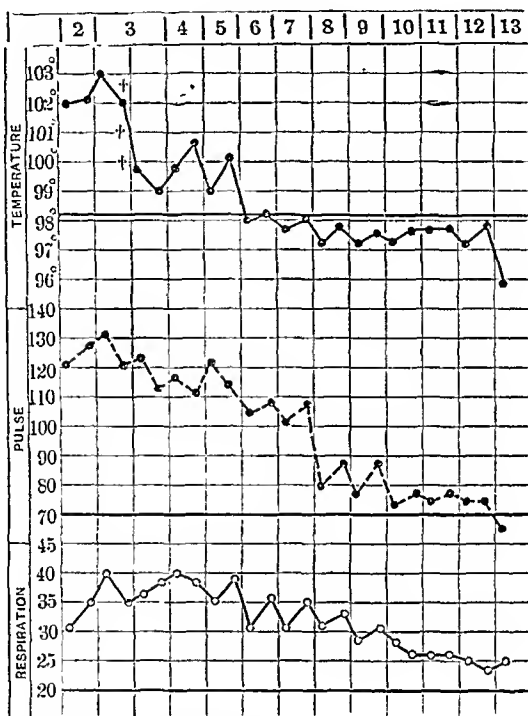
Percussion and auscultation signs, however, are uninfluenced. Even when the case is seen and treated comparatively early, dulness and bronchial breathing increase. The rules of resolution appear at the usual time, but not earlier. Involvement of new areas may take place during treatment, with return of symptoms, necessitating new injections. Pneumococcic empyema has occurred. The structural pathological processes, therefore, would appear to evolve

² Remarks on the Treatment of Pneumonia, by F. P. Henry, Phila. Med. Jour., February 14, 1903.

³ AMER. JOUR. MED. SCI., September, 1908.

in the customary manner, unmodified by the treatment, which is apparently not germicidal. Systematic and accurate quantitative observation of urinary chlorides is lacking, but a few approximations show no apparent deviation from the ordinary rule. Leukocytic studies as yet show nothing definite. A slight increase, not especially affecting any one variety, is the most common observation.

CHART I.*



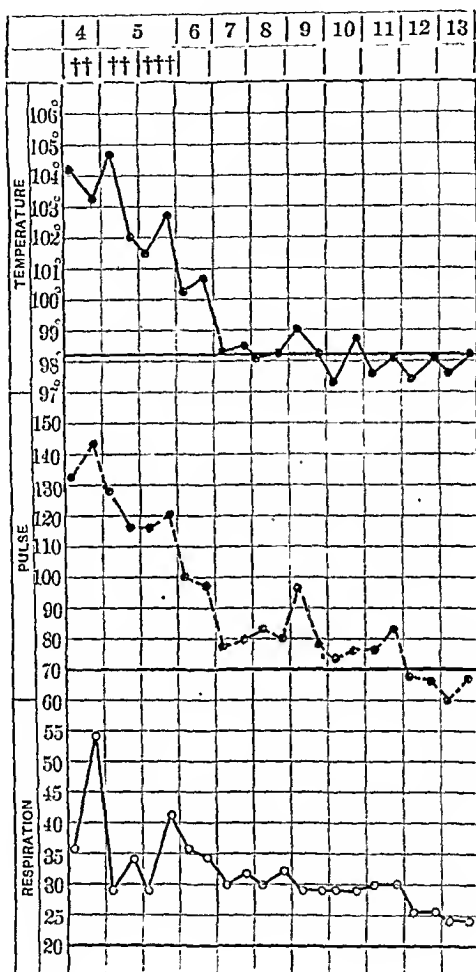
* The numerals at the top of the chart show the day of disease.

Abstract of Case, Chart I. Observations at first every four hours; then twice daily. *Acute lobar pneumonia; severe; left apex; alcoholic.* R. M., male, aged sixty years; laborer; colored. Chill; herpes; no jaundice; no vomiting; no delirium; slight cyanosis. Blood culture shows pneumococci. White blood cells, 24,000. †Three injections, 1 gram each; total quantity, 3 grams during twenty hours. First injection on third day; last injection on third day. White blood cells, 32,000 (increase 8000). Duration from chill to resolution, twelve days. Complication, pleurisy. Result, recovery.

The most striking results of the large doses of quinine are thus functional; and since the most significant features are the relief of respiration and the maintenance of normal cardiac vigor and blood pressure, it seems logical to infer that the effect is chemical and antitoxic. This view is further borne out by the absence of quinine intoxication, suggesting a mutual neutralization of disease-poison, and drug. It may be, however, that the antitoxic action is indirect; or that the drug acts, in part at least, as a direct stimulant to the autonomic cardio-respiratory centres. Experimental obser-

variations on this point are desirable, but the writer has thus far failed to arouse a sufficiently lively interest in any trained experimentalist.

CHART II.*



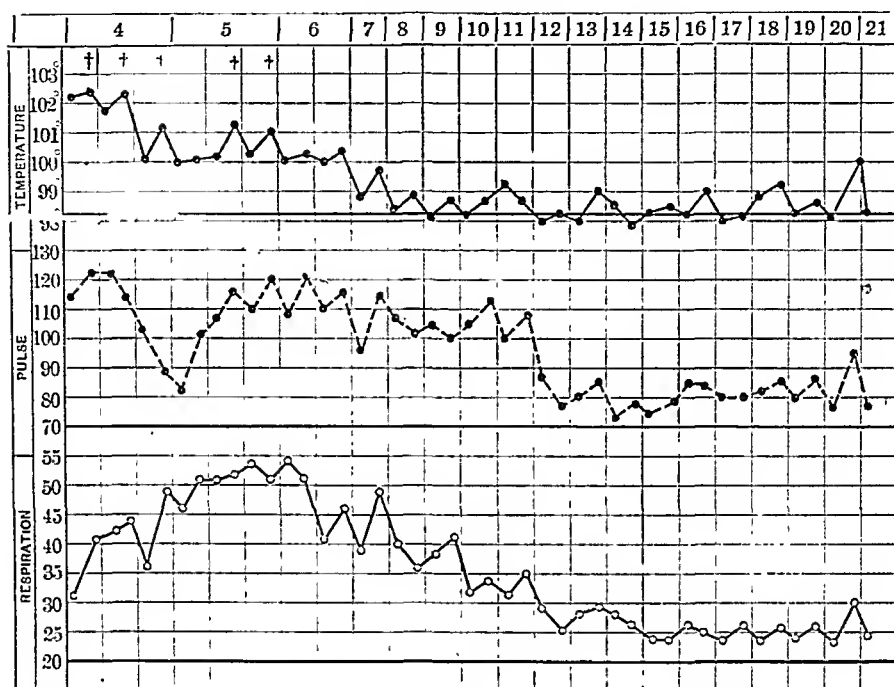
* The numerals at the top of the chart show the day of disease.

Abstract of Case, Chart II. Observations at first every fourth hour, then twice daily. *Acute lobar pneumonia; severe; right lower lobe.* S. S., female, aged fourteen years. Pneumococci in sputum; chill; no vomiting; no herpes; no cyanosis; no delirium. White blood cells, 14,000. †Seven injections, 0.5 gram each; total quantity, 3.5 grams in twenty-eight hours. First injection on fourth day; last injection on fifth day. White blood cells, 15,000 (increase 1000). Duration from chill to resolution, thirteen days. Complication, pleurisy. Result, recovery.

The total number of cases of acute lobar pneumonia thus treated and observed with sufficient accuracy for purposes of record was 87, with 16 deaths. Nearly all the deaths, however, occurred at the Philadelphia General Hospital, where the expected mortality of the unfavorable class of cases received is from 25 to 50 per cent., varying with the year. A much larger number of cases than that mentioned was treated by this method in the course of the

seven years that it has been carried out in the writer's hospital services, and more recently in private and consultation practice, with a total mortality of 12 per cent. (23 deaths in 192 cases). If alcoholic cases, terminal infections, pneumonia of the aged, patients over fifty years of age, and patients of all ages received on or after the third day of the disease, were excluded, the mor-

CHART III.*



* The numerals at the top of the chart show the day of disease.

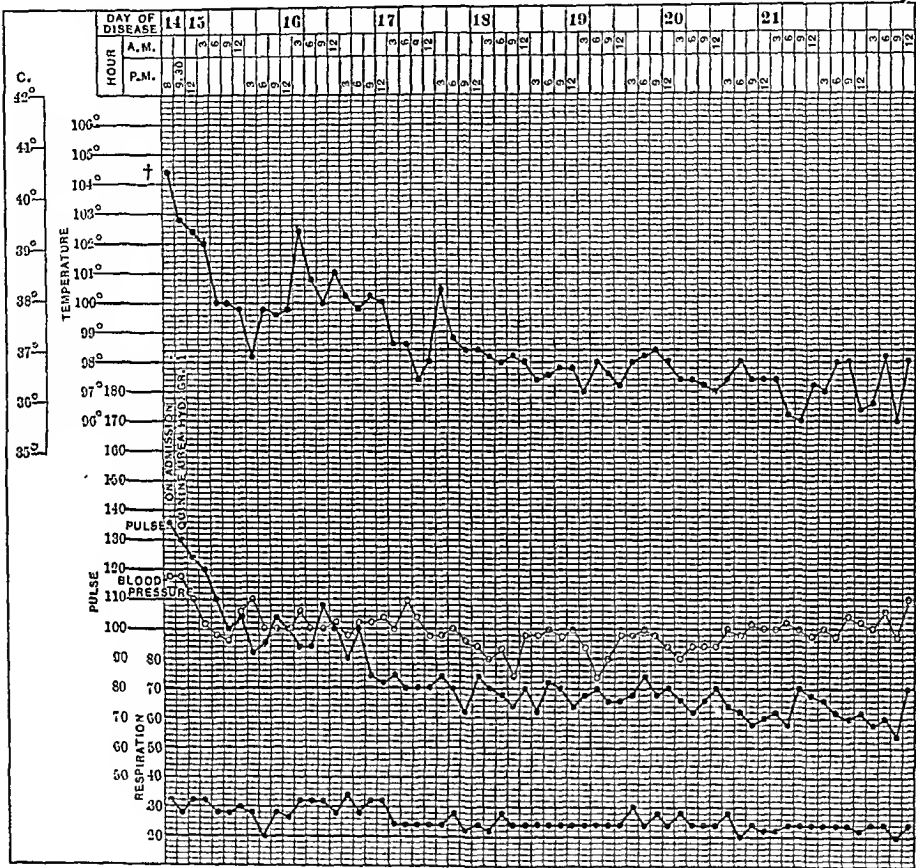
Abstract of Case, Chart III. Observations at first every fourth hour; then twice daily. *Acute lobar pneumonia; severe; right lung; left lower lobe.* S. St. L., male, aged twenty-eight years; seaman; black; not alcoholic; no venereal disease. Chill; cyanosis; delirium; no vomiting; no herpes; no jaundice. Pneumococci in sputum. White blood cells, 12,000. Urine contains pus, hyaline, and granular casts; chlorides diminished. †Five injections, 1 gram each; total quantity, 5 grams in sixty hours. First injection on fourth day; last injection on fifth day; fall of temperature after fourth injection. White blood cells, 20,000 (increase of 8000). Delirium abated; duration from chill to resolution twenty days. Complication, pleurisy. Result, recovery. It will be noted in this case that respiration continued to increase until after the fourth injection had been given. This was coincident with extension of the process in the right lung. Blood pressure, which is not shown upon the chart, was, however, favorably influenced from the beginning.

tality would be inconsiderable; but to exclude all of these cases would be to exclude also a large proportion of the recoveries. Even in fatal cases the patient's comfort was notably promoted.

While these studies were in progress, other cases were admitted to the writer's services and recovered without any special medication; the quinine treatment being reserved for cases in which decisive therapeutic intervention seemed necessary. Inclusion of the milder

cases among those treated would have lessened the mortality percentage. In the earlier observations patients admitted very late and in bad condition were not given quinine, and recovered or died under other plans of treatment. In the later experience, such patients also received the injections and usually with noticeably

CHART IV



Abstract of Case, Chart IV. Observations every third hour. *Acute pleuropneumonia (lobular), quite severe.* E. L., female, aged twenty-three years. Left upper and lower lobes; right middle lobe. Cyanosis. Not alcoholic; no venereal disease; no chill; no delirium; no vomiting; no herpes; no jaundice. Sputum contains a few gram-positive diplococci, many streptococci and staphylococci. Admitted fourteenth day. Blood pressure below pulse frequency. †One injection, 1 gram. Prompt fall of temperature, pulse, and blood pressure. Subsequent rise of blood pressure beyond pulse frequency. White blood cells, 15,000. Duration to complete resolution twenty-four days (ten days after injection). Result, recovery.

good results. In no case was a bad result observed that could be attributed to the drug. While the statistics of recovery suffered, many individuals got well that otherwise might have perished.

In addition to the use of the quinine salt, fresh air, water, and all other necessary measures of good nursing were provided; and such agents as strychnine, digitalis, alcohol, camphor, opium, cocaine, epinephrin, musk, and alkaline diuretics were administered when

symptomatically indicated. Special attention was paid to the consonance of pulse rate in beats per minute with systolic blood pressure, measured in millimeters of mercury, as advised by G. A. Gibson,⁴ of Edinburgh, and by Hare,⁵ excess of the number representing frequency over that representing pressure thus measured, being met by appropriate medication. In a number of cases saline infusion was also used, and in some of these, oxygen as well; the latter measure chiefly as a palliative in the fatal cases, as in those cases which ran a favorable course it did not often seem to be necessary. In the cases treated during the last two years, sodium bicarbonate or ammonium compounds were given in sufficient quantity to keep the urine alkaline throughout the course of the attack, and this seems to have been of benefit. Following Galbraith's plan, tincture of ferric chloride was given when the quinine was withdrawn. Lobular pneumonia was influenced favorably in a similar manner to lobar pneumonia.

Four charts are selected for reproduction as illustrative of different types of cases.

In *making the injection*, the following precautions, published by the writer in 1887, and several times since, must be observed; otherwise there may be cellulitis, slough, or abscess. The syringe is filled with a 50 per cent. solution of the quinine and urea salt in sterilized water; and the needle is inserted deeply, through skin previously painted with tincture of iodine, into a muscle. The syringe is emptied thoroughly, so that solution does not drop upon the skin when the needle is withdrawn. The point of puncture is sealed with iodoform-collodion. Thousands of injections have been made in this manner without ill-result of any kind.

BRONZED DIABETES. REPORT OF A CASE WITH SPECIAL REFERENCE TO THE INVOLVEMENT OF THE PANCREAS IN DIABETES.

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THE following case when first seen was readily diagnosticated as an example of that rare symptom complex or combination of diseases picturesquely named by the French "Bronzed Diabetes."

⁴ Edinburgh Med. Jour., January, 1908, lxx, 22; G. A. Gordon, Ibid., January, 1910, n. s. iv, p. 37.

⁵ Therap. Gaz., 1910, xxxiv, 397.

The patient was closely followed for an extended period of time, and in this way provided an excellent subject for the study of the various manifestations of the disease. Our clinical and pathological observations are therefore of considerable value to the literature upon a subject in which theoretical considerations have generally overbalanced the account both of the clinical course and of the postmortem abnormalities. A careful examination of the sections of this patient's pancreas stimulated one of us to further study into the intricate connection between this organ and diabetes, and led to some tentative conclusions at variance with what is generally accepted.

The case was as follows: A male, aged fifty-five years, a timber merchant, first came under observation in March, 1908, on account of weakness, loss of weight, irritability, and increased frequency of urination. There was also slightly increased thirst. For several months he had been constantly testing his urine for glucose, and was much depressed when any was demonstrated. Increased frequency of micturition was first noticed six years before while traveling in Spain. He gained weight for several years, and until four years ago weighed 247 pounds. At that time he began to feel lazy and tired. Two years ago, when traveling up the Nile, eating considerable sweets and drinking 1 or 2 pints of champagne daily, the patient again noted increased frequency of urination and increased amount of urine, especially at night, and glycosuria was demonstrated. Since January 1 of this year his diet was rather strict. The amount of urine varied from 50 to 75 ounces daily, and with Hayne's test 3 to 4 drops produced a reduction. He has been upon a more or less strict antidiabetic diet ever since, with intervals of disappearance of sugar from the urine. For the last three years he has been annoyed by cough, expectoration, slight, gradually increasing dyspnea, and cold hands and feet. He was told by a physician that he had a "spot on his lungs."

Family History. Married; no children; wife never had miscarriages; father died suddenly, aged fifty years, of "rheumatism and heart disease;" mother died, aged sixty-four years, of "Bright's disease;" grandfather died, aged ninety-eight years, of "diabetes." One younger brother is subject to "muscular rheumatism."

Habits. He used alcohol very moderately until five or six years ago. Since then he has taken a pint of wine and one or two whiskies daily. He uses tobacco—6 cigars, an occasional pipe, and 10 or 12 cigarettes daily. He has been a large eater for the last ten years. He is fond of sweets, but rarely eats them to excess.

Past History. Venereal diseases denied. No evidence of syphilis. "Sunstroke" twenty-five years ago (during very hot weather), fell suddenly from moving car, struck back of head, lost memory for few days; "neurasthenia" for one year afterward. He did not

feel perfectly well after this for six or seven years. He is not subject to headaches. Mild attack of gout twenty years ago. Subject to occasional attacks of "biliousness," and twice vomited large quantities of "partly digested blood." Hemorrhoids never noted. He has traveled extensively in hot countries, but has never had malaria. Consulted dentist frequently during last ten years for trouble with his gums. Has been taking veronal for insomnia. He has never taken arsenic or silver, so far as he knows, nor has he been subject to any affection of the skin.

Physical Examination. Height, 6 feet 1 inch; weight, 200 pounds; nutrition fair, abdomen prominent. Color of face deep brown and somewhat cyanotic. Mucous membrane of mouth brownish blue in color. Tongue dry, red, fissured, and clean. Gums bled easily. Pharynx dry and congested. Teeth irregular and decayed. Breath, slightly sweetish odor. Wrists, fingers, and hands brownish-blue color, palms reddish. The legs and feet were pale yellowish brown, cold, and cyanotic, and the veins rather prominent. Skin of the body was pale yellowish brown, soft, smooth, delicate, and distinctly dark for a blond man. The superficial and deep reflexes were normal.

Heart. Dulness slightly increased both to left and right. The aortic second sound was accentuated. There were no murmurs.

Lungs. Nothing abnormal detected.

Spleen. Enlarged, easily palpable at costal margin.

Liver. Upper border in fourth space in right midclavicular line; lower border hard but smooth, palpated three fingers' breadth below costal margin in right midclavicular line.

No special enlargement of abdominal veins and no ascites. No glandular enlargement.

Urine. 3600 c.c. in twenty-four hours. It contained 18.5 grams of sugar, no acetone, a slight trace of albumin, and occasional casts.

Progress of Case. During the next four months the sugar in the urine from time to time disappeared altogether, and the amount of urine varied between 1500 c.c. and 2900 c.c. On one occasion the quantity of urine reached 4400 c.c. in twenty-four hours and contained 33.75 grams sugar.

November, 1908. The color, particularly of the face and dorsum of hands, had deepened. In the axillæ and around the genitals there was considerable dark pigmentation. This was not patchy, nor was there any leukoderma. There was a more or less sharply defined line of demarcation between the neck and wrists, and the adjoining body surface. The margin of pigmentation of the dorsum of the feet showed only a gradual transition. The palms were of a reddish blue without any brown tint. There was no ascites or edema. There was a short systolic murmur at the apex, but no increase of the cardiac enlargement. The gums were still markedly swollen and bled very readily, although they

had been thoroughly treated by a dentist. The temperature always remained normal or subnormal.

November 10, 1908, to January 25, 1909. Urine on an average amounted to 3500 c.c. per day, but varied between 1550 c.c. and 6800 c.c. The amount of sugar varied between 340 grams in twenty-four hours to as low as 4 grams. On only one occasion, no sugar was demonstrated. Acetone was almost constantly present. A trace of albumin and casts were also usually found.

Urinalysis.

November 11, 1908.		January 22, 1909.	
Amount	3360 c.c.	6505 c.c.
Specific gravity	1025	1011
Albumin	0	0
Indican	0	
Sugar	3.7 per cent.	0.8 per cent.
Total	124.5	48.6 g.
Acetone—			
Diacetic acid	0.318 gram acetone	0
Beta-oxybutyric acid	0.47 gram	0
Total nitrogen	26.10	14.62
Gross urea nitrogen	19.64 = 75.3 per cent.	10.80 75.4 per cent.
Net urea nitrogen	18.00 = 69.0 per cent.	9.88 69.0 per cent.
Ammonia nitrogen	1.64 = 6.3 per cent.	0.917 6.4 per cent.
Kreatinin nitrogen	0.725	0.420
Kreatin nitrogen	0.07	0.206
Uric acid nitrogen	0.425	0.114
Rest nitrogen	5.24 = 20.1 per cent.	3.08 = 21.1 per cent.
Total food: carbohydrate, 50 grams;		January 21, milk day.	
Fat, 300 grams; protein, 150 grams		Total food: carbohydrate,	
		55 grams;	
		Fat, 50 grams; protein,	
		40 grams	

During this period he suffered from insomnia and attacks of facial neuralgia. In December, 1908, edema of the legs and ascites gradually developed.

April, 1909. Coughed up about a pint of blood, dark at first, then bright red. Ascites marked. No change in lungs, heart, liver, or spleen. Urine on an average contained 3 to 8 grains sugar to the ounce, and always some acetone and diacetic acid. The bronzing of the skin had become much more marked.

May, 1909. Developed a phlebitis of left saphenous vein which gradually subsided. Sciatica in both legs had also become very troublesome. There was also at this time periarthritic and arthritic swelling and tenderness of the right shoulder, hips, knees, and ankles. Upon a low carbohydrate and low protein diet, poor in salt, and with the help of free catharsis every few days, the edema and ascites gradually diminished.

December, 1909. Extremely edematous, abdomen very prominent from ascites. Heart considerably dilated and with long musical systolic murmur in the apex region. Blood pressure, 130. Bronzing of the skin much the same, but slightly more leaden in color.

Blood: Hemoglobin, 97 per cent., red blood cells, 4,760,000. White blood cells, 8900. Polymorphonuclears, 47 per cent.

Urine: (December 15) 1600 c.c. in twenty-four hours contained 109 grams sugar. Temperature always normal or subnormal.

January, 1910. Improved considerably with rest and dieting.

April 8, 1910. Ascites very marked again. Became incontinent of urine and feces. Urine contained pus, blood, and a considerable quantity of albumin and casts. The sugar content was 4.6 per cent. with no accompanying acetone bodies.

April 10, 1910. Died comatose.

The *autopsy* on this case was conducted six hours after death. Development and nutrition were fair. There was slight edema of the feet and marked protrusion of the abdomen from ascites. The skin showed a general faint brownish discoloration especially obvious on the back of the hands, the axillæ, the genitals, and the face, in which situations it also had a somewhat bluish tinge; and was associated with a considerable roughening and scaly appearance. The mucous membrane of the mouth was a faintly yellow color, as if from jaundice. There were no other skin lesions and no enlargement of the superficial lymphatic glands. The left pleural cavity contained about two pints of clear, slightly blood-tinged fluid. The right pleura was universally adherent.

The *lungs* were grayish in color, edematous, and congested, the lower lobe on the left side being somewhat collapsed.

The *heart* was slightly dilated and the myocardium, particularly of the left ventricle, somewhat atrophied and that of the right side considerably infiltrated by fat. The heart muscle was dark brown in color and very friable. The mitral valve admitted three fingers and the tricuspid five. There was slight thickening of the aortic and mitral orifices, but no endocarditis. The coronary arteries were considerably sclerotic near their orifices and the aorta was markedly atheromatous.

There was no smooth atrophy of the base of the tongue and no important change in the esophagus.

The *abdominal cavity* contained about 8 quarts of a yellowish, slightly turbid fluid. This was found to contain a small number of pus cells and a culture of staphylococcus albus.

The intestines were extremely distended and very edematous. The peritoneum was somewhat thickened, and on its surface were scanty patches of fibrinous exudate.

The *liver* was enlarged and showed coarse granulations on the surface and in its interior. It was dark brown in color, particularly in the parenchymatous islets. The fibrous tissue intersecting these islets was in considerable amount, dense, and congested. The gall-bladder was slightly dilated, its walls thin, and it contained no stones. The bile ducts were pervious throughout.

The *pancreas* was very small, densely embedded in fat so that

it could not be shelled out. It was extensively replaced by fibrous tissue, particularly marked in the middle of the body, where relatively little pancreatic tissue remained. The pancreatic lobules and to a less extent the intersecting fibrous tissue were dark rusty brown in color. No stones were found in the pancreatic duct.

The *kidneys* were slightly enlarged and showed a condition of cloudy swelling, but practically no chronic nephritis. They were yellowish brown in color, evidently also the seat of some pigmentation. In the cortex of both kidneys there were several small pyogenic abscesses, and the pelves of both kidneys were inflamed and contained a small amount of thin purulent material.

The *urinary bladder* was slightly dilated and was filled with a thin pus. Its walls were slightly thickened and its lining membrane inflamed and showed numerous hemorrhages.

The *lymphatic glands* in the abdomen showed no special enlargement, but on section were reddish brown in color, as if pigmented like the other organs.

The *brain* was very edematous. The vessels at the base, however, were only slightly atheromatous. With these exceptions there were no obvious gross lesions in any part of the brain.

Microscopic Examination. The skin in its deeper layer was the seat of a considerable deposit of granular yellow pigment, which for the most part gave the reaction of hemosiderin. The true skin was slightly atrophied and the stratum corneum considerably thickened. In the subcutaneous tissues no inflammatory condition could be observed.

The liver showed a condition of old-standing cirrhosis. The fibrous-tissue strands were well-defined, densely fibrous, and not particularly broad. The liver-cell masses were also sharply outlined and the liver cells had an irregular trabecular arrangement. The deposit of pigment in the liver was very extensive. It was chiefly massed in the liver cells and in slightly greater amount toward the periphery of the parenchymatous islets. In the individual liver cells the pigment was aggregated especially in the centre of the cell or toward the middle of the trabecula. The pigment was composed of small granules of more or less uniform size, bright yellow in color, and gave rapidly the iron reaction of hemosiderin. Some of the pigment granules, however, failed to give this reaction, thus resembling the hemofuscin described by von Recklinghausen. The pigment was not deposited in especially degenerate cells, and was in relatively small amount in the fibrous-tissue tracts. It was found in the lining cells of bile ducts, but practically no free pigment was contained in their lumen. The lymphatics in the fibrous areas in the liver commonly contained heavily pigmented mononucleated cells.

In the larger vessels in the portal spaces there were generally to be found a few isolated small granules of pigment among the red

blood corpuscles. These free granules in the bloodvessels were not in very large amount, and their presence in this situation did not appear to be the result of any artefact. Although it seems as if these granules were formed in the blood and secondarily deposited in the tissues, yet it is possible that mechanical postmortem influences, or a discharge of granules into the blood from the tissue cells may have been responsible for the appearance of pigment in the bloodvessels.

The spleen was in a condition of advanced venous stasis. The intersinus pulp cells were also somewhat hyperplastic, and the interior of the venous sinuses was frequently filled with mononucleated cells, evidently the result of some reactive process. Pigmentation in the spleen was relatively small in amount, although the cells lining the sinuses and in the intersinus tissue could commonly be seen containing small granules of yellow pigment.

The abdominal lymph glands showed slight hyperplasia of the lymph cells, but no necrosis or fibrous-tissue formation. As in the spleen, mononucleated cells were fairly frequently observed to contain granules of iron pigment.

The intestines in their submucous layer were considerably thickened by chronic inflammatory change. The mucosa was considerably atrophic. In the subepithelial tissues there was a particularly large number of small eosinophile cells. All of these changes, however, are not peculiar to the disease and may be found in any case of advanced liver cirrhosis.

The kidneys presented no evidence of chronic nephritis. The glomeruli and convoluted tubules were well preserved. Only a very small amount of pigment was found in the convoluted tubules and in the intertubular connective tissue.

The heart muscle cells were considerably atrophied, and the majority were loaded with the same granular pigment, chiefly hemosiderin, which was found in other organs.

The thyroid showed the usual spaces filled with colloid. Most of these spaces were comparatively small and some showed slight hyperplasia of the lining cells. In this situation also there was a very considerable amount of pigment in the cells lining the spaces and a small amount also among the colloid material.

The lungs showed chronic congestion and edema and only a very slight degree of pigmentation.

The brain in the cerebral cortex and in the region of the medulla showed no special histological change except slight edema. The nerve cells in the medulla occasionally contained a small amount of the same pigment found in the other organs, but did not appear in any way degenerated.

The pancreas was very extensively replaced by inflammatory tissue and by fat. The vessels in the interior of the organ showed no special change, and the ducts, although catarrhal, were not

dilated or obliterated by fibrous tissue. The parenchyma seemed to have been largely destroyed, but the portions which persisted among the inflammatory tissue were isolated as small rounded groups of acini (Fig. 1). Indeed, at first sight, all that seemed to have been spared were islands of Langerhans. The majority of these pancreatic remnants, however, were obviously acinous tissue, yet many also were definite islands of Langerhans. These latter, indeed appeared to be in considerable number, and many of them were well preserved. For the most part, they were larger

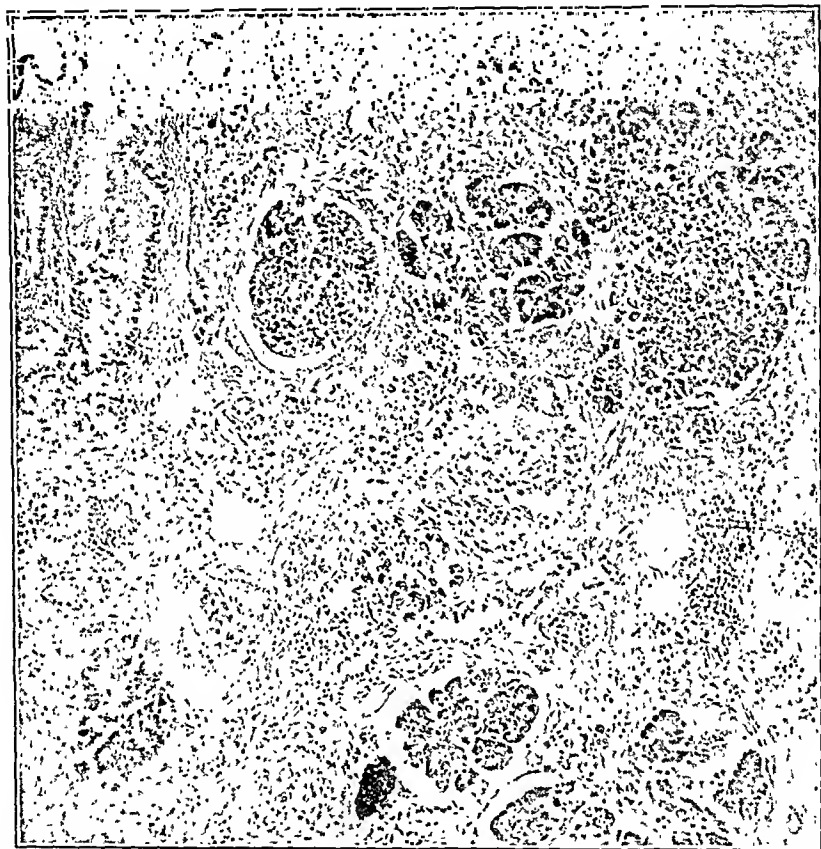


FIG. 1.—Pancreas from a case of bronzed diabetes, showing persistence of small remnants of pancreas tissue, many of which, although definitely acini, might be mistaken for islands. $\times 150$.

than normal, although their number probably was less. In many places there were clumps of cells where it was almost impossible to differentiate between acinous and island tissue (Fig. 2). Isolated groups of acini seemed to become catarrhal, their cells became smaller, until structures apparently indistinguishable from islands were produced.

These transition figures in the pancreas, although they can only be accepted with some reservations, are particularly interesting, and are perhaps, sufficiently important to warrant a short digression into the morphology of the pancreas and its relation to diabetes.

The islands of Langerhans since their discovery in 1869, have provided a source of very varied discussion and their function is still uncertain. Numerous elaborate works on this subject have recently appeared, and most of them, Dewitt's,¹ for example, contain a very complete review of the literature. In these works

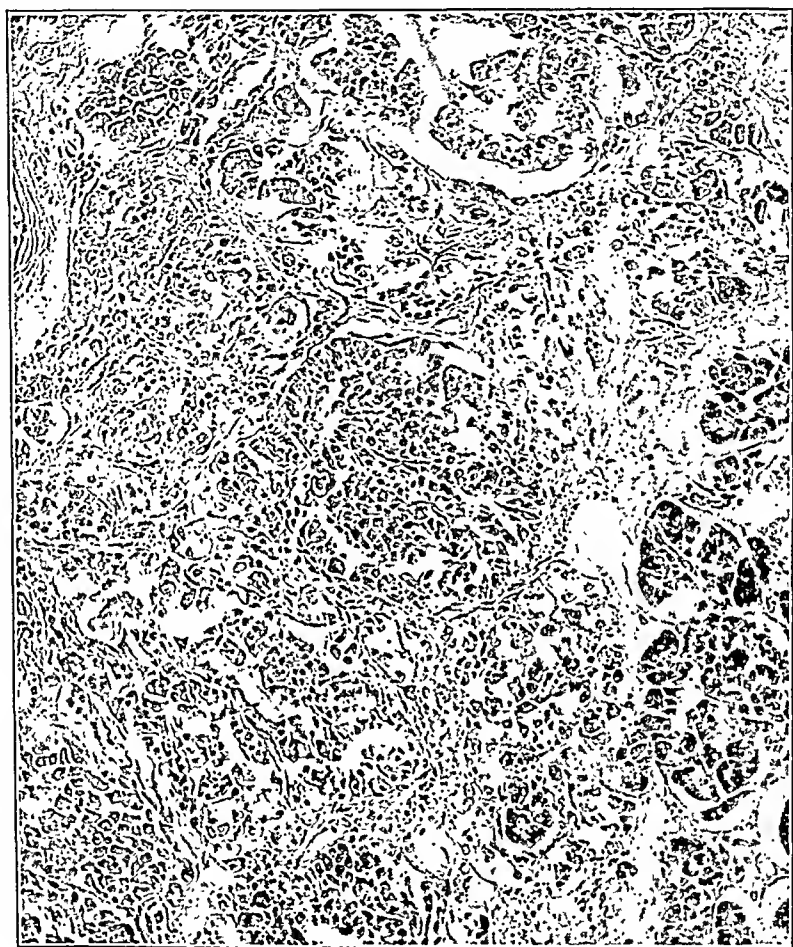


FIG. 2.—Pancreas from a case of bronzed diabetes. The parenchyma is divided into small groups, some of which resemble both acini and islands. $\times 190$

the anatomy of the pancreas and the vascular arrangement and structure of the islands of Langerhans are fully described. It is perhaps sufficient here to note that they were originally thought to be nervous elements. They have been considered by Hanse-
mann² as mesodermal in origin, and a number of the earlier authors³ described them as lymphocytes. It has been shown, however,

¹ Jour. of Exp. Med., 1906, viii, 193.

² Zeit. f. klin. Med., 1894, xxvi, 191; Verhandl. der deutschen path. Gesellsch., 1902, iv, 187.

³ Dieckhoff, Krause, Kuhn and Lea, Mouret, Pischifger, Pugnât, Renault, Sokoloff.

that the islands are derived originally from pancreas tissue. Kuster⁴ described them as arising from the ducts, and Pearce⁵ from the acinous tubules. Laguesse⁶ also concluded that they were derived from the acinous tissue, but that they were transitory and might later assume the appearance of acini. The islands seem to be more numerous in the embryo than in the adult; thus, they have been considered as embryonic remains.⁷ They also have been described as exhausted acini⁸ and as acini changed temporarily, but which were capable of reverting back.⁹ Minkowski has expressed the opinion that the number of islands increases during the period of activity of the pancreas and diminishes during the period of rest, and that every lobule at some time must pass through a "Stadium der Langerhans'schen Inseln."

The general opinion, however, and that which is included in practically all the recent works on this subject,¹⁰ is that the islands are absolutely independent structures and elaborate some internal secretion. It is a peculiarly attractive theory and one which is supported by the very definite outline of the islands, as well as their more or less constant shape and number.

It is generally admitted that there are extensive variations in size, shape, and number of the islands; the type of their component cells and their arrangement are also by no means regular in different cases and even in adjacent islands of the same pancreas.

The following pictures are included as illustrative of some of these variations in the human pancreas (Figs. 3 to 11).

These pictures not only seem to show great individual variations in the islands, but also are suggestive of their mode of formation. Figs. 3, 4, 6, 7, and 10, appear to indicate that the islands are not always absolutely independent structures. Indeed, in almost every human pancreas, and even more commonly in the pancreas of rabbits, very intimate connections can be observed between the island trabeculae and adjacent acini. By serial sections such connections may be demonstrated in some situation in practically every island. This may of course, be argued as a persistence of the original fetal connection.

In a large number of cases the capsule outlining the island is very indistinct, or absent, or may only be represented by a capillary. This capsule has been described as a special structure, but often groups of pancreas acini are surrounded in an exactly similar manner (Fig. 8). Indeed, the whole circulation in many

⁴ Arch. f. mik. Anat., 1904, lxiv, 1.

⁵ Amer. Jour. of Anat., 1903, ii, 445; Amer. Med., 1903, vi, 1020.

⁶ Compt. rend. de la Soc. de Biol., 1894, xlv, 667; Jour. de l'anat., 1894, xxx, 591; Compt. rend. de la Soc. de Biol., 1895, xlvii, 699; Jour. de l'anat., 1896, vol. xxxii, Compt. rend. de la Soc. de Biol., 1905, lviii, 504; Ibid., 1905, viii, 542.

⁷ Gibbs, Harris, and Gow.

⁸ Dogiel, Tschassownikow.

⁹ Kollossow, Laguesse, Lewaschew, Minkowski, Saviotto, Statkewitsch.

¹⁰ Diamare, Jarotsky. v. Ebner, Opic, Schultze, Sobolow, Sauerbeck, Lépine.

of these islands might be reconstructed from interacinous vessels which have become dilated in consequence of some atrophy of the

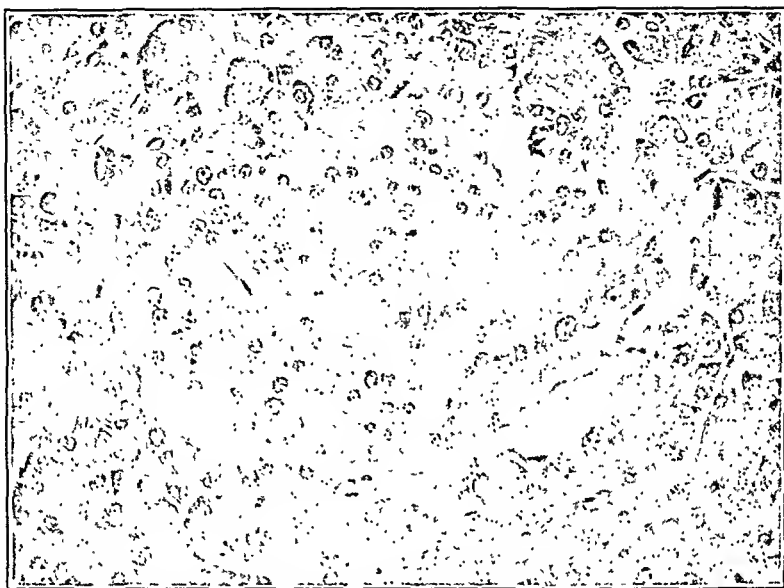


FIG. 3.—Island of Langerhans, composed of large cells arranged in trabeculae, some of which are intimately related with the adjoining pancreas acini. (From a male, aged thirty-three years; died from pneumonia.) $\times 400$.

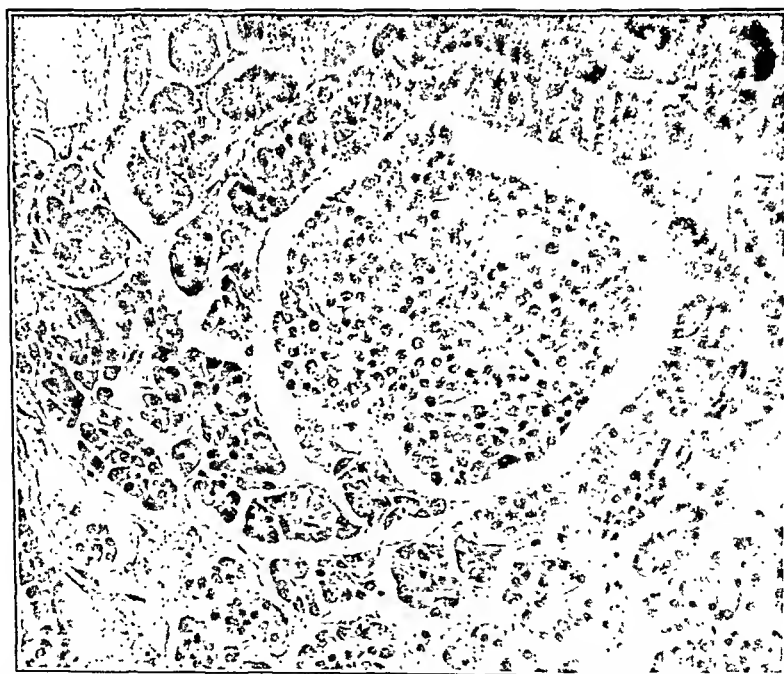


FIG. 4.—Island of Langerhans, composed of a solid mass of cells, which are, however, grouped in small masses. (From a female, aged thirty-seven years; died of mitral stenosis and thrombosis of the jugular and subclavian veins on the left side.) $\times 400$

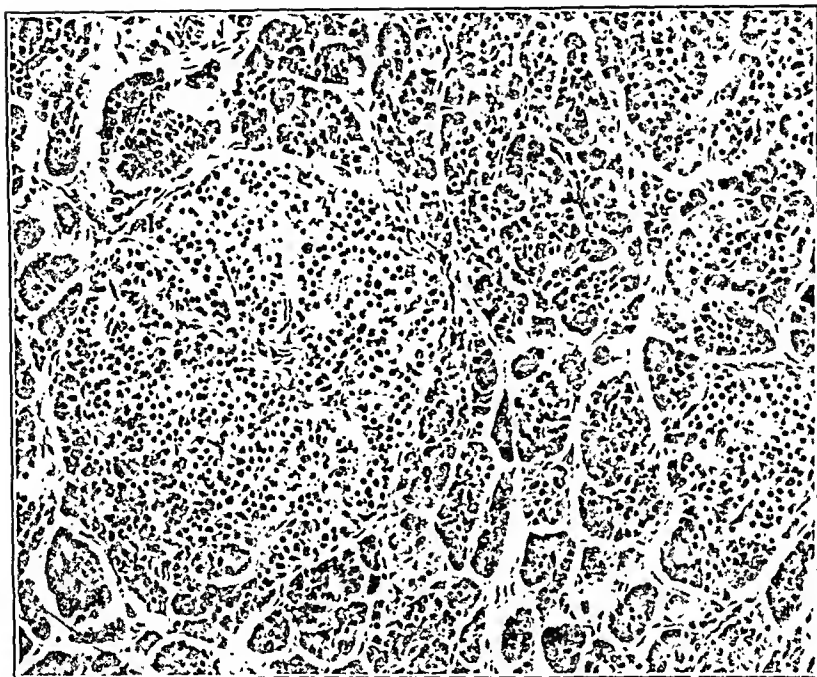


FIG. 5.—Large adenomatous island. Several of the pancreas acini show intimate relations with cell groups closely resembling islands. (Pancreas of a male, aged sixty-three years, weight, 121 pounds. Aorta slightly atheromatous. Died of acute general peritonitis following herniotomy operation.) $\times 230$.

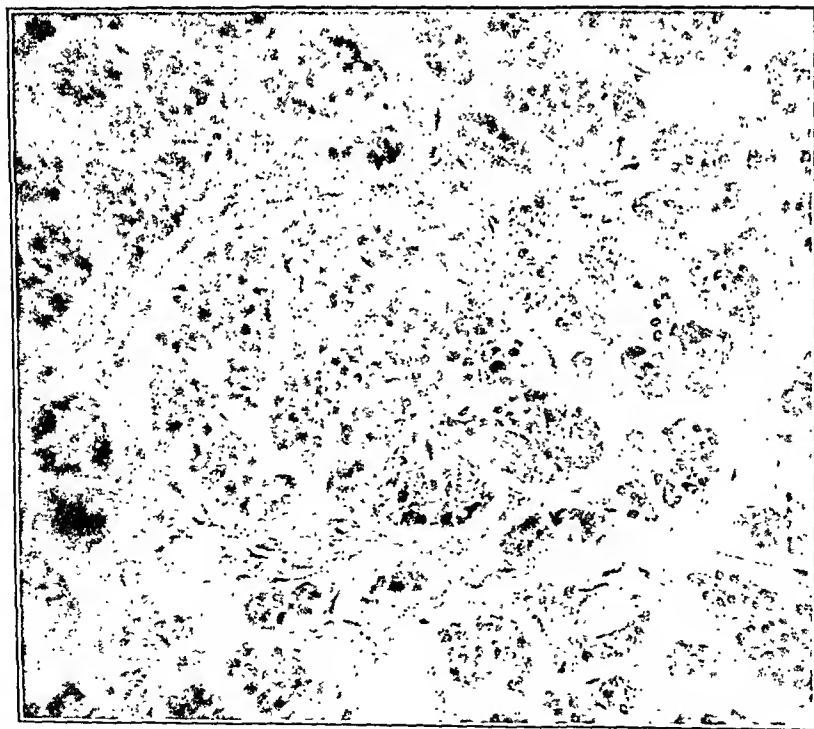


FIG. 6.—Island showing inclusion, within the capsule, of acinous-looking cells. (From a female, aged sixty-four years; died from a cardiac atrophy. No edema or cyanosis.) $\times 400$.

acinous cells. In contradiction to what is usually noted, it might even be said that the circulation in the islands of Langerhans shows no essential difference from that in the rest of the pancreas.

The cells composing the islands commonly are arranged as a single layer along the vessels, but very frequently also the island has an acinous appearance (Figs. 4, 5, 9, and 10), and sometimes also the whole space is filled with cells with no particular arrangement (Fig. 4). In many cases portions of definitely acinous tissue are included among the island cells, an appearance which must not be confused with irregular islands extending among the acini (Figs. 6, 7, and 10). Apparently, also, there are very sugges-

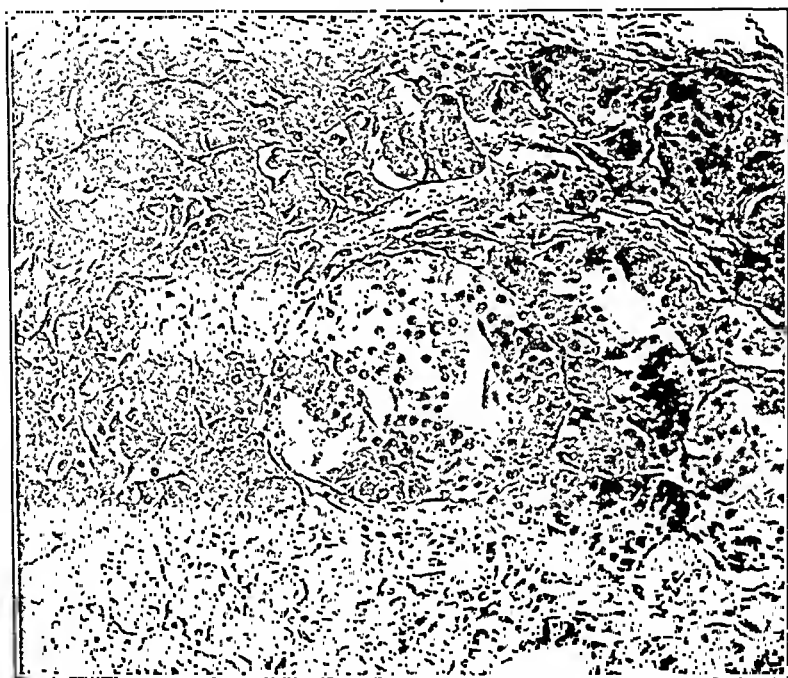


FIG. 7.—Island showing inclusion of definitely acinous cells intimately related to the island cells. (From a female, aged forty-nine years; died of mitral stenosis and gangrene of left leg from thrombosis.) $\times 280$.

tive indications that in such cases the island cells are being formed by a catarrhal atrophic process from the acini (Fig. 6). Frequent pictures, however, are to be noted where the island cells are apparently becoming swollen and darker in their staining reactions and arranged more like ordinary acinous cells (Fig. 10). Mitoses have been described in the island cells, but in all our material none were found.

There are therefore, some indications, in contradiction to those who maintain the independent existence of the islands, that these structures have both intimate relationships with the pancreas acini and also that transitions in adult life are a distinct possibility.

Although these transition figures have been noted by a variety of writers, it has generally been considered that even if new islands are formed in the adult pancreas, they are developed for some function relating to carbohydrate metabolism.

This also has considerable interest in relation to the etiology of diabetes, as Opie,¹¹ Weichselbaum and Stangl,¹² Wright and Joslin,¹³ Herzog,¹⁴ Sobolow,¹⁵ and many others accept the theory as justified



FIG. 8.—A group of pancreas acini isolated like islands. (From a male, aged fifty-nine years, weight, 119 pounds. Extensive arteriosclerosis. Died of a hypernephroma of the right kidney with metastases in the bones, brain, lungs, etc.) $\times 400$.

that diabetes may be due to some change in the islands. Indeed, the relation of the islands of Langerhans to carbohydrate metabolism has largely been originated by the pathological reports of these investigators, particularly by Opie and those others who have described cases of diabetes with lesions in the islands alone. Cecil,¹⁶ for instance, of 90 cases of diabetes, found 79 in which the

¹¹ Jour. Exper. Med., 1901, v, 397, 527.

¹² Wiener klin. Woeh., 1901, xiv, 968.

¹³ Jour. of Med. Research, 1901, vi, 360.

¹⁴ Virchow's Archiv, 1902, clxviii, 83; Trans. of Chicago Path. Soc., 1901, v, 2.

¹⁵ Ibid., 1902, clxviii, 91.

¹⁶ Jour. Exp. Med., 1909, xi, 266.

islands were either hyaline or sclerotic, and in 12 of these the remaining pancreas was not especially affected. If it is admitted, however, that the islands of Langerhans are either undifferentiated or regressive pancreas acini, it is just such tissue which most likely would be affected by hyaline or sclerotic changes. The pancreas also is well known to be subject to extremely rapid postmortem change in consequence of which small patches of degeneration may be produced which very closely resemble the changes described in the pancreas of some diabetics. Indeed, the great bulk of pancreas autopsy material is useless for examination, and postmortem changes have to be very carefully considered in every case.

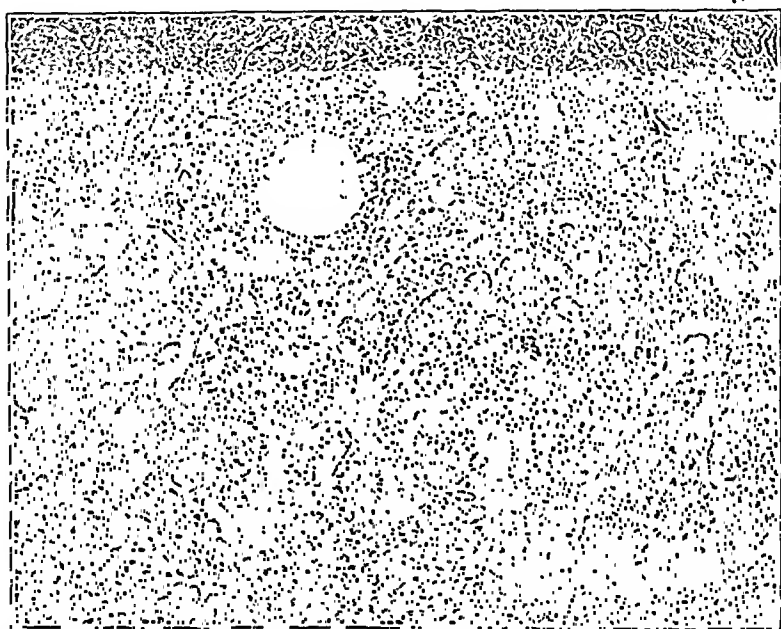


FIG. 9.—Pancreas showing a variety of types of islands. To the left an island is adenomatous in type; in the centre, an island contains almost typical acini. (From a male, aged sixty-six years; weight, 139 pounds; died from mitral stenosis, general venous stasis, and hydrothorax.) $\times 90$.

A particularly strong argument for the island theory has been advocated from the results of ligature of the pancreatic duct. In such conditions, as is well known, there occurs extensive atrophy of the pancreas, and eventually, as is claimed by many observers, only islands of Langerhans persist. It has also been noted that ligature of the pancreatic duct is followed only very rarely by any glycosuria. Vassali (1891) was perhaps the first to perform this experiment. He noted a general glandular atrophy, but with preservation of the islands. In 1900 Schultze¹⁷ confirmed this, ligating off small portions of the pancreas in guinea-pigs. After eighty

¹⁷ Arch. f. mik. Anat., 1900, lvi, 491.

days he found only a few dilated ducts and normal islands. Since no glycosuria was produced his natural conclusion was strongly in support of the independent existence and internal secretion of the islands. Zunz,¹⁸ in 1905, produced apparently the same condition in the pancreas of dogs. In 1901 Minkowski,¹⁹ from similar experiments, concluded that the pancreatic tubules and islands both become atrophied as a result of the operation, and

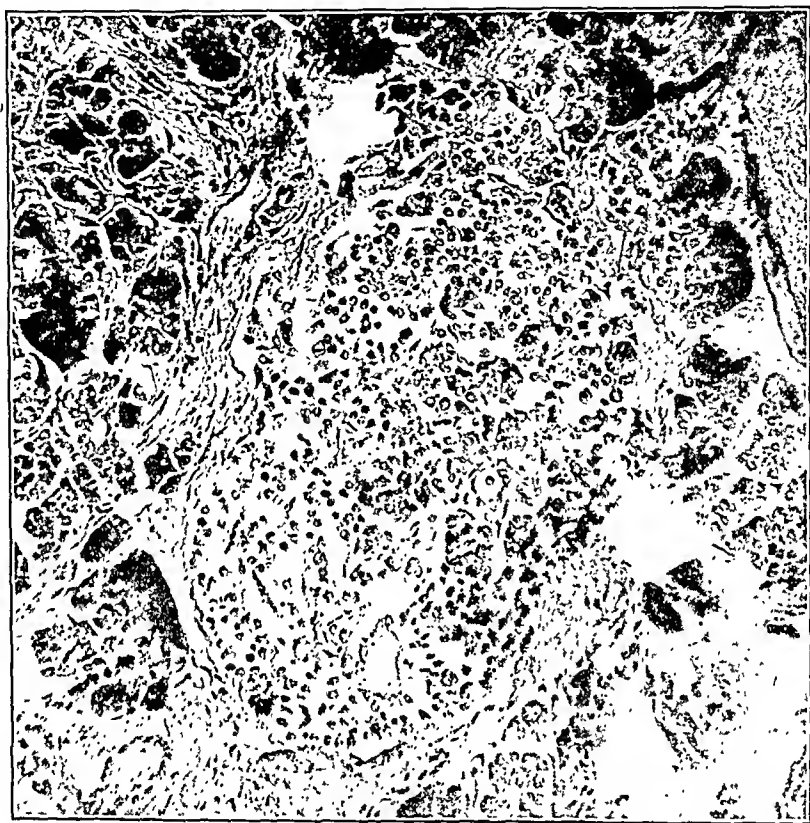


FIG. 10.—Large island of Langerhans, showing within it enlargement of some of the cells with acinous arrangement of these, like the formation of new pancreas acini. (From a male, aged forty-eight years; died of *tuberculosis dorsalis*.) $\times 280$.

Hansemann²⁰ (1902) had the same results. Excretory channels of the pancreas apparently tend to be readily reformed, and, as Dewitt²¹ notes, this may account for the contradictory results obtained after ligature of the duct. The operation in many cases, as noted by Hansemann (1902) and Lombroso (1905),²² does not by any means cause atrophy of the entire pancreas, so an absence of glycosuria is not conclusive evidence of the island theory.

¹⁸ Zeit. f. allg. Path. u. path. Anat., 1905, xvi, 5.

¹⁹ Arch. f. mik. Anat., 1901, lix, 286.

²⁰ Loc. cit.

²¹ Loc. cit.

²² Arch. ital. de biol., 1904, vol. xlii; Jour. de Phys. et de Path. gén., 1905, vii, 3.

Our own experience of the effects of ligature of the pancreatic ducts in animals is limited to 5 cats, 2 rabbits, 2 guinea-pigs, and 1 dog. In these animals the pancreas was ligatured at the point where it is reflected from the duodenum. So far as possible care was taken to avoid the bloodvessels, so that the result might not be modified in this way. In all of these much the same changes were produced. Even after forty-eight hours in a guinea-pig definite atrophic changes were found in the acini. After four days the atrophy of the acini was marked, but many of the islands could

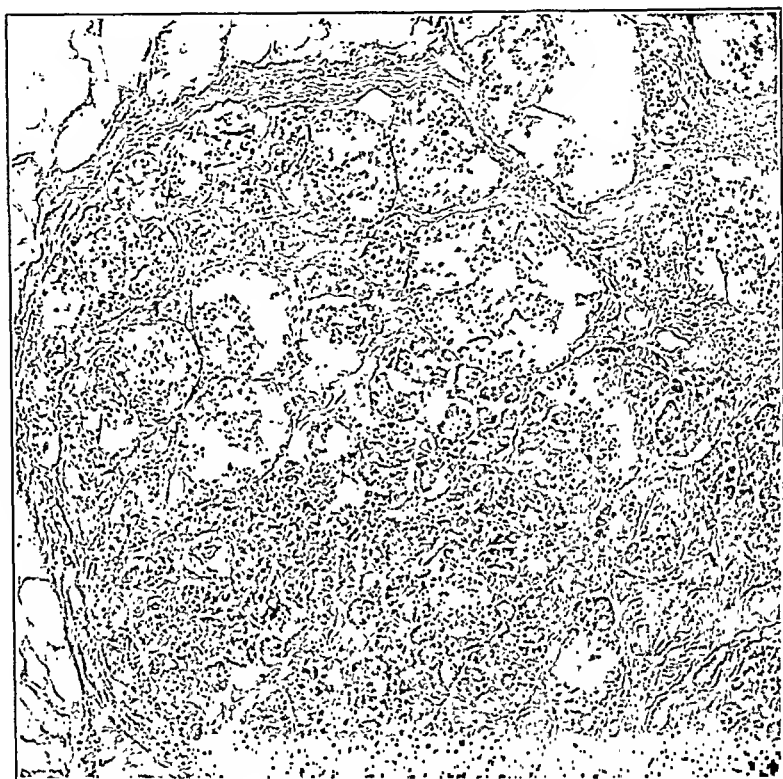


FIG. 11.—Section of a pancreas which seems to be almost entirely composed of islands. (From a female, aged forty-nine years, 105 pounds in weight. No arteriosclerosis. Died of mitral stenosis and gangrene of the left leg, probably from thrombosis.) $\times 80$.

still be seen persisting in the atrophic lobules. In three weeks the acinous tissue had become very attenuated. It was isolated in small masses surrounded by fibrous tissue and no islands were distinguishable (Fig. 12). Both the islands and acini seemed to undergo a similar atrophy. No glycosuria was found in any case. There were, however, in some of the cases, particularly in the dog which was killed 9 weeks after the operation, occasional patches of healthy looking pancreas tissue which seemed to have escaped the atrophic process and which may have been responsible for the non-development of glycosuria. The persistence of comparatively small

portions of pancreas tissue is sufficient to prevent glycosuria. In dogs no diabetes results if only a narrow strip of pancreas tissue is left along the duodenum. In the cats, at any rate, there seemed to be no special preservation of the islands, and all that appeared to remain in the older standing cases were sub-groups of atrophied acinous cells.

It is also a difficult fact to explain why in a considerable proportion of diabetics, the islands are considerably reduced in number or may even be absent altogether. In one of our cases of a rapidly fatal diabetes in a man, aged thirty-five years, after a search through the greater part of the pancreas no islands were found. The pancreas acini in this case were extremely atrophic. This is at first

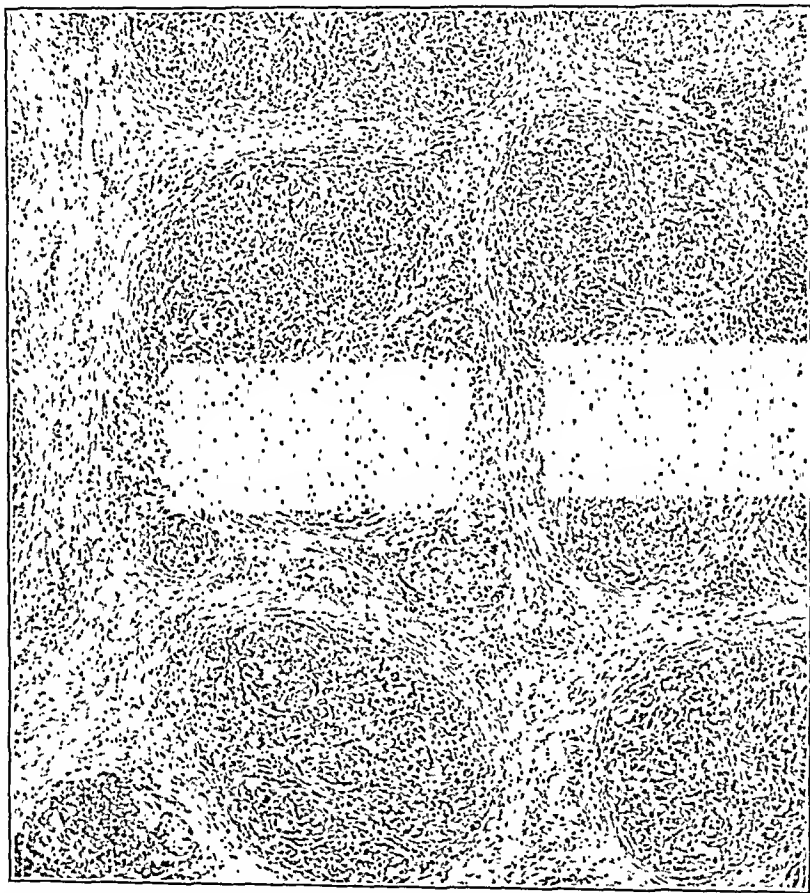


FIG. 12.—Pancreas of a cat whose pancreatic duct had been ligatured three weeks previously. The acini have become collapsed and atrophic. There has been an extensive development of fibrous tissue. No islands of Langerhans can be found among the atrophic acinous tissue. $\times 90$.

strongly in support of the island theory, yet if these islands had been leading an independent existence some scars or necrotic remnants ought to remain indicating the positions where the islands were destroyed. These, however, were not noticeable.

It has thus also to be considered as possible that the islands are a reserve source for the formation of new pancreas tissue, and also that pancreas acini may revert in type to structures resembling or identical with Langerhans' islands. There are, then, a number of facts which are difficult to reconcile with the island theory and such observers as Hanseemann,²³ Gutmann,²⁴ Reitmann,²⁵ Karaschew,²⁶ Herxheimer,²⁷ Dieckhoff, Benda, and others have unhesitatingly condemned it. It is certainly difficult to credit the islands, whose total amount is so relatively small, and whose component cells at least appear to be so poorly specialized, with one of the largest functions in the metabolism of the body.

However one regards the etiology of diabetes, involvement of the pancreas has become the most important factor. It is diseased in the great majority of cases. In Cecil's²⁸ series of 90 cases it was described as unaffected in only 6. There is, however, no constant lesion in the pancreas which is associated with diabetes, as the pathological changes vary from general atrophy which in some cases is the result of arteriosclerosis, to necrosis and fibrous replacement of the organ. Hanseemann²⁹ also has described 12 cases of diabetes due to occlusion of the pancreatic duct by stones. Similarly, gallstones impacted in the ampulla may also induce diabetes on account of marked inflammatory change in the pancreas, probably resulting from regurgitation of the bile salts into the pancreatic ducts.

It seems possible, therefore, that the pancreas is not merely an organ secreting digestive enzymes, but, in its entirety, has also important relations in carbohydrate metabolism. The pancreas does not seem to have any special relation to the formation of glycogen, as it has been shown that glycogen is formed in diabetes. Nischi's³⁰ work is confirmatory of this, as he injected glucose solution into one-half of the liver of depancreatized tortoises and found that the glycogen content of the injected half was greatly increased. It may be, of course, that the pancreas involves some internal secretion which regulates sugar destruction, yet, even more likely, it eliminates or destroys substances which when accumulated in sufficient degree by retention in the system, on account of deficient pancreas activity, are capable of producing abnormal disintegration of glycogen, etc., in the tissues and consequent diabetes. In support of this it has been shown by the researches of Arnheim and Rosenbaum, and by Feinschmidt, after removal of the pancreas in dogs, and apparently also in human diabetes, that the serum and tissues

²³ Loc. cit.

²⁴ Virchow's Archiv, 1904. clxxvii, Suppl., Heft 128.

²⁵ Zeit. f. Heilkunde, 1905, xxvi. 1.

²⁶ Deutsches Arch. f. klin. Med., 1904, lxxxii, 60.

²⁷ Verhandl. der deutschen path. Gesellsch. Ergänzungsheft; Cent. f. path. Anat., 1904, xv, 215.

²⁸ Loc. cit.

²⁹ Loc. cit.

³⁰ Arch. f. Exp. Path. u. Therap., 1909-10, lxii, 173.

contain abnormal amounts of a glycolytic substance. Lépine (1905)³¹ also observed after ligation of the pancreatic duct or injection of oil into it that the glycolytic power of the blood is greatly increased.

The serum of depancreatized dogs does seem to possess a considerably increased ability to convert glycogen into dextrose, as compared with normal serum.

Evidence is not yet complete enough to conclude that pancreas insufficiency is the primary factor in every case of diabetes, yet even at the present time it has assumed by far the most important place.

The relation of the liver to diabetes, if any, is difficult to understand. The symptom complex *Bronzed Diabetes* has been adduced by many writers to support the theoretical existence of a so-called "liver diabetes;" but a careful study of the reported cases hardly warrants such an assumption. Certainly lesions of every conceivable type and severity can affect the liver without the production of any glycosuria. In Simmond's³² series of 144 cases of diabetes only 7 had liver cirrhosis. Those cases in which liver cirrhosis has been associated with glycosuria are, as Steinhaus, Lando, and others have shown, also cases in which the pancreas has been extensively diseased.

The possibility of cerebral diabetes is difficult to dispute. Undoubtedly lesions of the medulla are associated with glycosuria; but only very few diabetics show any demonstrable lesions in the brain. Vasomotor changes in the pancreas, as influenced through the centre in the medulla, may be the essential factor. Such conditions as fright may markedly increase the sugar output in a diabetic (an evident feature in our case); and adrenalin injections in animals may produce glycosuria. Both of these factors profoundly alter the vasomotor system and may act on the pancreas in this way.

It, of course, cannot be denied that they might not act similarly on the so-called sugar controlling centre of the brain, although Herter's observation that painting adrenalin on the pancreas was associated with glycosuria much more rapidly and extensively than by any other mode of administration, is somewhat contradictory.

To Hanot and Chauffard, in 1882, belongs the credit of having first noted the disease condition known as bronzed diabetes, although some years previously Trousseau³³ had reported the autopsy on a diabetic with a bronzing of the face and nearly black discoloration of the penis, and found a greatly enlarged cirrhotic liver of a grayish-yellow color; and Troisier, in 1871, described a case under the title of "diabète sucré."

³¹ Compt. rend. de la Soc. de Biol., 1903, lv, 161; Jour. de Phys. et de Path. gén., 1905, vii, 1.

³² Berl. klin. Woch., 1909, xli, 531.

³³ Clinique méd., 2d edition, ii, 627.

The symptom complex which they described had a triad of symptoms—pigmentation of the skin, cirrhosis of the liver, and diabetes. These, however, do not occur simultaneously and cases are described varying in every way as to the primary event. The present-day opinion seems still to agree with that of Hanot, Marie, and others of the earlier authors that bronzed diabetes is not a mere modification of diabetes, but a true pathological entity.

The bronzing is perhaps the most conspicuous sign. It is due to the deposit of pigment, mostly hemosiderin, but partly non-iron containing, in the tissues. This variety of pigmentation was originally termed hemochromatosis by v. Recklinghausen in 1889. It is a blood derivative, yet the degree of anemia, if any, is, as a rule, very slight. On account of this relatively slight anemia it has been considered that there is, as Meltzer has advocated, a defective elimination of normally destroyed blood. There certainly must be defective elimination of some sort, because the liver in practically every case of hemochromatosis has been described as diseased in one way or other. A number of cases (8, 7, 14, 17, 28, 32, 39, 40, in list) have been described, it is true, by various observers where there have been hemorrhages in some situation or other during the disease. This, however, is not the rule, and is no more than can be observed in any series of liver cirrhosis cases. Unfortunately we did not procure a specimen of the bone marrow from our case, but in the sections of the various organs there was no evidence of blood regeneration. The sections of bone marrow in one of Sprunt's cases showed "practically a normal picture;" in the other the marrow was "slightly hyperplastic, but there was nothing to indicate any unusually active hematopoiesis."

Probably, however, there is also some excessive blood destruction, as the accumulation of pigment is often enormous, and in some cases it has been very extensive within a short period. Generally the destruction of blood must be slowly accomplished to permit of the more or less complete regeneration and the high blood counts usually recorded.

The general opinion (Jeanselme, Berg, Buss, Anschutz, Doutournier, Marie, etc.) seems to be, as expressed by Fletcher, "that the pigmentation of the viscera is primary and antedates the diabetes," and "that the deposition of the hemosiderin in the cells of the liver and pancreas and of the hemofuscin in the connective tissues of these glands eventually leads to the large, cirrhotic, pigmented liver and the sclerotic pancreas, which are so characteristic of the disease."

This idea of hemochromatosis being the primary event is neither easy to understand nor to prove. It presupposes blood destruction from some unknown cause. Clinically, in Fletcher's second case, as in several others, the first sign was pigmentation, but considering the well-known latency of symptoms of many diseases, notably

cirrhosis of the liver, it is impossible to be certain that the blood destruction and pigmentation are the primary events.

There is undoubtedly a deposit of iron containing pigment in the tissues in many other diseases, as pernicious anemia. Hintze³⁴ has described 5 cases of extensive hemosiderin pigmentation of the viscera in tuberculosis and carcinoma, and Goebel³⁵ has noted a similar condition in a case of carcinoma of the stomach. Tillmanns³⁶ described a case of a man, aged seventy-six years, who died two months after having sustained a fracture of the pelvis and a ruptured liver, and at whose autopsy a general hemochromatosis of the viscera was found. Osler also has noted pigmentation of the skin in 6 out of 15 cases of splenic anemia. In exophthalmic goitre also, there frequently is found some excess of cutaneous pigmentation, and its distribution is about the same as in bronzed diabetes cases.

In cases of bronzed diabetes the only constant, co-existing, anatomical lesions seem to be hepatic cirrhosis and sclerosis of the pancreas. In some of the recorded cases the liver has simply been noted as enlarged. Most of these probably were cirrhotic, although it must be remembered that in many diabetics the liver is enlarged from fatty change. Glénard noted that the liver was enlarged in 32 per cent. of all diabetics. These two organs have been thus blamed for the production of the hemochromatosis. Brault and Gaillard have considered the liver cirrhosis as primary and the blood degeneration as a result, and Kretz stated that the liver disease and blood destruction were coördinate events. Hess and Zurhelle also have noted the liver cirrhosis as primary, then the hemochromatosis, and finally diabetes. Rössle³⁷ believed that the blood destruction was due to a capillaritis and an abnormal phagocytic activity of the liver cells, and the pigment thus produced by the blood destruction in the liver was disseminated to the other organs. Rössle's work is, however, by no means convincing. Undoubtedly, blood cells are commonly found in various pathological conditions in the liver cells, but mostly in a degenerate state. It is also difficult to imagine any spontaneous sudden phagocytic activity of the liver cells for red cells alone, and if it did occur, why hemochromatosis should be so rare.

Osler, Opie, and others have advocated that the pigment is formed in the liver and disseminated from it to the other organs. Létulle, although holding that diabetes was the primary factor, claimed that the pigment was formed where it was found deposited.

Beattie also, although not claiming any phagocytic activity for

³⁴ Virchow's Archiv, 1880, lxxix, 492.

³⁵ Ibid., 1894, cxxvi, 482.

³⁶ Arch. d. Heilkunde, 1878, xix, 119.

³⁷ Ziegler's Beiträge, 1907, xli, 181.

the liver, stated that the pigment is elaborated in the liver and pancreas and disseminated from there, and by its irritation was responsible for at least some of the fibrosis in these organs.

Diabetes has been considered by many, particularly Hanot and Schachmann, Hernandez, Mossé, Massary, and Potier, to be the primary condition and the source of the blood destruction and hemochromatosis. Diabetes, however, only very rarely is associated with hemochromatosis. Fitcher notes that of 256 cases of diabetes, only 2 were bronzed. Also a number of authors—including Létulle, 2 cases; Brault, 2; Osler,³⁸ 2; Opie,³⁹ 1; Abbott,⁴⁰ 1, and Hintze, 3 cases—have described hemochromatosis and liver cirrhosis unaccompanied by diabetes.

The suprarenals have been claimed to have important relationships to the production of hemochromatosis. Blum,⁴¹ as the result of his being able to produce glycosuria by adrenalin injections, came to the conclusion that lesions of the suprarenal played an important role in the production of bronzing of the skin in some cases of diabetes. The suprarenals were noted as abnormal in the cases of Mossé and Daunic, and of Rabé, and it has been contended that hemochromatosis is due to some defective control of pigmentation by the suprarenals. With the exception of Rabé's case, where the adrenals were tuberculous, the changes in the suprarenals described in the above cases were only what might be found in any autopsy. Neither the cutaneous nor visceral pigmentation of hemochromatosis appears to be in any way allied to that of Addison's disease.

The clinical record of the present case is of some value in the time relation of the pigmentation, as it did not appear until some years after evidences of liver cirrhosis and symptoms of diabetes had appeared. It must, however, be remembered that the skin in hemochromatosis is probably the last site to be pigmented. In the cases of Wille, Kretz, and Létulle there was extensive pigmentation of the internal organs, but none was noted in the skin. In many cases the pigmentation evidently either escapes observation or is regarded as merely the result of exposure to the sun's rays, and so fails to attract especial attention. In our case it had not been noted by other physicians previous to our first examination, and the patient's wife had supposed his color was nothing but sunburn. Neither the family physician nor the family had noted any pigmentation in Blumer's case. The pigmentation of the skin is always much less than that of the other organs.⁴² It may

³⁸ Brit. Med. Jour., 1899, ii, 1895.

³⁹ Diseases of the Pancreas, 1910, p. 368.

⁴⁰ Trans. Path. Soc., London, 1900, li, 66.

⁴¹ Deut. Arch. f. klin. Med., 1901, lxxi, 146.

⁴² In Abbott's case (without diabetes and the only unquestioned case of hemochromatosis in a woman) the skin pigmentation was very slight.

be that before the skin pigmentation becomes obvious clinically, exposure to sunlight and the production of some dermatitis is necessary. It is certain that in most bronzed diabetes cases, the pigmentation is chiefly on the exposed part of the body.⁴³ Possibly this accounts for the fact that almost every case of hemochromatosis with skin bronzing has been described in males. The greater opportunity for exposure and the natural dryness, as well as the greater tendency for dermatitis, may account for the bronzing in general hemochromatosis to be almost exclusively in males. In addition, the type of cirrhosis commonly described in hemochromatosis is also relatively more frequent in males. Besides Abbott's case, in a woman without diabetes, Berg⁴⁴ and Murri have also published female cases, but of these, Berg's case later came to autopsy, and there was no mention of hemochromatosis, and Murri's case exhibited pediculi and was discharged with normal skin and normal urine.

The pathological records of our case argue against the theory that the pigment accumulation is the cause of the inflammatory process in the various organs because the pigment evidently was largely deposited in the spared parenchyma cells of the liver and pancreas, and to a relatively much less extent in the connective tissues of these organs. The kidneys, thyroid, heart, etc., were all extensively pigmented, yet were hardly at all involved in any cicatricial process. It is doubtful, indeed, if blood pigment has any marked tendency to cause inflammatory processes. Hematoidin certainly seems to exist in large amount in the liver cells and in the heart muscle without producing any extensive damage in these organs.

In almost every case of liver cirrhosis there is some iron-containing pigment in the liver cells, and often a small amount in the other organs also. This is only natural when one considers that liver cirrhosis is caused by some toxic process which at the same time might readily cause blood destruction. Also, the accumulation of substances not eliminated by the liver may be a source of considerable hemolysis. The rarity of general hemochromatosis in sufficient degree to cause skin bronzing can only be explained by assuming that only rarely is there sufficiently extensive blood destruction in liver cirrhosis.

The relationship of diabetes to liver cirrhosis seems more easily established. In from 2 to 4 per cent. of all cases of liver cirrhosis

⁴³ Whether the pigmentation ever diminished in intensity upon lack of exposure to the sun cannot be stated. In our case the bronzing lessened, but the grayish-blue color increased as time went on and the patient was more confined to his room and bed. In a second case which we have studied, and which has not yet been proved by autopsy to be a case of hemochromatosis, there has been a very marked change, since his weakened condition and later occupation have kept him most of the time within doors; in fact, the pigmentation has practically disappeared. In Murri's the pigmentation cleared up during patient's two years residence in hospital.

⁴⁴ Med. Rec., 1899, lvi, 881.

there is diabetes, and of all diabetics about 5 per cent. are associated with signs of liver cirrhosis. In such combinations there is not necessarily any hemochromatosis. Barth,⁴⁵ for instance, has described such a case without any pigmentation. As Steinhäus,⁴⁶ Lando,⁴⁷ and others have shown, and in our own experience, the pancreas is commonly involved in liver cirrhosis cases. The pancreas may become damaged by the same process which causes the liver cirrhosis, or it may also be that the catarrhal processes so common in the bile ducts in liver cirrhosis may involve the excretory channels of the pancreas and induce secondary atrophic and sclerotic changes in that organ. Sprunt considers hemochromatosis to be "a metabolic disease implicating many of the body tissues and manifested, especially, by a change in the chromogenic groups of the proteid molecule with the deposition of pigments." He refers the diabetes to the diminished oxidative power of the body due to pronounced disturbances in the iron containing constituents of the tissues, assuming these iron compounds to be catalytic agents in oxidizing processes." Much further clinical and experimental investigation must be carried out before the chromogenic groups of the protein molecule are held accountable for this condition, and still more to interpret the cause of the change. As far as the etiology of hemochromatosis has been studied nothing very helpful is to be learned from the previously recorded cases. Infections which might be responsible for the blood destruction, such as tuberculosis, sepsis, parotitis, and pyorrhea are very frequent in the described cases, but hardly commoner than terminal conditions in diabetes and cirrhosis of the liver. Malaria also is noted in a number of the cases, yet could not be considered an important etiological factor. Excess of alcohol is mentioned as a possible cause in a large proportion of cases, but in several it had no connection whatever.

From what may be gathered in the literature and from the study of our own case, it would seem as if today we are warranted in stating only that cirrhosis of the liver is the primary condition; that pancreatic involvement with diabetes is a sequence or coincident event to this; that the hemochromatosis, always in slight degree in liver cirrhosis, is in some cases very excessive and causes a general pigmentation which eventually also involves the skin; and finally, that the whole process is not any definite symptom complex, but a chain of circumstance which rarely seems to be completed.

⁴⁵ Bull. Soc. Anat., 1888.

⁴⁶ Deut. Arch. f. klin. Med., 1902, lxxiv, 557.

⁴⁷ Zeitschr. f. Heilkunde (Path. Anat.), 1906, vol vii

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A second case of writers', male, aged forty-nine years, pigmented four years, skin section contained pigment giving iron reaction. Diabetes, two years. Liver much enlarged and nodular. Ascites, two years.

REPORT OF A CASE OF LOUD VENOUS HUM HEARD OVER
THE XIPHOID CARTILAGE IN CIRRHOSIS OF
THE LIVER. AUTOPSY.¹

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MURMURS heard in the epigastrium in cirrhosis of the liver have been observed by many clinicians. Most of these have been of venous origin, and, being more or less confined to the region of the umbilicus, have been thought to be due to enlarged umbilical or para-umbilical veins. In some instances such conditions have been proved by autopsy.

The case of which the following is a history is of great rarity, and I have found but two similar ones on record, though in neither of these was an autopsy obtained, so that the anatomical similarity must remain conjectural. W. S. Thayer² reported a case under the following heading: "Report of a Case of Venous Hum heard in the Epigastrium in a Case of Cirrhosis of the Liver," and his study of the literature, from which I quote, yielded but one other case in which the murmur was similarly situated, and in which the same theory might account for the phenomenon.

The case here reported came under my observation in the wards of the Philadelphia Hospital on the service of Dr. F. P. Henry.

The history of the patient is as follows:

W. T. J., aged seventy years, male, stone cutter, machinist, and watchman.

Family history of no significance.

Social History. The man gives a history of excessive use of alcohol for a long period of years. Takes whiskey and beer frequently, and has been accustomed to the taking of whiskey on an empty stomach in the early morning.

Previous Medical History. Thirty-five years ago he had a severe attack of articular rheumatism, confining him to bed for some six weeks. Since that time he has had numerous more or less similar attacks. Four years ago the patient was confined to his bed suffering from dyspnea and edema of the extremities.

Present Illness. His present illness dates from a period about four months ago, when he noticed that he tired easily and became short of breath on exertion. Three months ago he was compelled to give up work of any kind. The dyspnea has gradually grown

¹ Read before the Medical Section, College of Physicians, Philadelphia, May 11, 1911.

² AMER. JOUR. MED. SCI., March, 1911.

worse, and he is now unable to go about. Two months ago he noticed his abdomen was swollen.

Physical Examination. Chest is emphysematous in appearance. The abdomen is full, and two veins stand out conspicuously, running more or less parallel from the middle of each groin, and anastomosing at a point between the umbilicus and ensiform, and a little to the left of the median line. Here there is a large varicosity from which a number of veins spring and travel upward over the ribs and sternum, and may be seen as high as the second rib. These veins empty with inspiration, and seem also to have another rhythm, possibly in some relation to the cardiac cycle. Pulses are equal.

Percussion over the lungs is normal except for a wooden note. Auscultation is negative.

The heart shows a little hypertrophy, and a systolic murmur is heard at the apex as well as at the aortic cartilage, the latter being transmitted into the carotid arteries. Over the ensiform cartilage is heard a very loud roaring murmur, which is localized to an area scarcely exceeding the space covered by the head of the stethoscope. This murmur is continuous, but has remissions in its loudness, there being a distinct inspiratory accentuation and a corresponding expiratory lessening. The murmur can be readily made to disappear by light pressure of the stethoscope. The liver dulness is apparently about normal, although a slight quantity of fluid and gaseous distention of the abdomen interferes with accurate determination of the lower border of liver dulness. There is some edema of the ankles.

The subsequent history in brief was that on May 7, 1911, the man rather suddenly became delirious and very ill, and on May 12, 1911, died of pulmonary edema. There was no increase of the ascites, which at no time reached large proportions, a fact possibly due to the free venous anastomosis. The roaring murmur, however, disappeared altogether for a time, but was faintly heard afterward.

Autopsy. At my request the prominent superficial veins were injected with a starch solution colored with methylene blue. An unsuccessful attempt was also made to inject the internal mammary vein.

The following notes are taken from the autopsy record in part, and the more minute description of the sinus was given me by Dr. McConnell, who made the autopsy.

Just beneath the ensiform cartilage are dense adhesions to the anterior margin of the liver. Within this mass of adhesions is a large venous sinus, the branches of which pass down into the adhesions. The spleen is bound down by adhesions. Elsewhere the peritoneum is smooth and transparent.

Heart. Aortic leaflets rigid and contain deposits of lime which extend well up from the bases of the leaflets.

Liver. This organ is small and pale, with a markedly roughened surface. It is firm and cuts with difficulty, leaving a granular surface. On section the surface is gray, with small brown areas scattered throughout.

Gall-bladder. This is greatly distended; full of thick, brown fluid. The cystic duct is obstructed.

Underlying the ensiform cartilage and extending to the articulation with the sternum there is found a venous sinus about 7 mm. in diameter. Anteriorly there could be seen through an opening in the ensiform the anterior wall of this sinus. Proceeding from this opening were several small, superficial veins, probably in communication with the sinus. From this sinus there was a vein communicating with the vein in the suspensory ligament of the liver; this latter was somewhat dilated. Apparently there was no communication between the portal vein or inferior vena cava.

The entire lesion was contained within the mass of adhesions, between the anterior portion of the liver near its edge and the overlying ensiform and lower part of the sternum. The area occupied by the mass was about 4 by $2\frac{1}{2}$ c.m.

These continuous loud murmurs are usually of venous origin, and are supposed to originate from small veins flowing into larger ones. The sound in this case must have been transmitted from the sinus to the surface by the small veins which perforated the ensiform and approached the surface.

The extreme localization of such a surprisingly loud sound was interesting and difficult to explain, unless due to the fact that the sinus was not in direct contact with conducting surfaces, being buried in a mesh of adhesions. For the same reason, perhaps, no thrill was present. It was impossible to identify this mass with any known vessels. It was apparently not connected with the vein of the round ligament, which in turn was enlarged.

The author suggested the possibility of the sinus being an anomalous ductus venosus, but such a theory could not be proved, as careful dissection was impossible.

Charcot is authority for a statement that venous hums in cirrhosis of the liver are of favorable portent, and one might be tempted to go farther and form a corollary to this proposition by stating that the disappearance of such murmurs is of evil omen. In our case, and also in Thayer's, the disappearance of the murmur meant the beginning of dissolution.

TUBERCULOSIS AMONG PHYSICIANS.

WITH REPORT OF ONE HUNDRED CASES.

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I HAVE been under the impression for a long time that physicians fare rather better than the average patients among the laity when attacked with pulmonary tuberculosis. This study of the disease in 100 physicians who have been under my care during the last fifteen years is intended to test the correctness or falsity of this impression. Theoretically, the prognosis among medical men should be better than in others because of their familiarity with the earlier indications of the disease, and their knowledge of the supreme importance of early and correct treatment. For the same reasons those failing to obtain complete restoration to health should yet live longer than average lay patients.

In this tabulation no cases have been included in which the disease was so recent in origin as to make its classification as to possible recovery open to serious doubt. The 100 cases have naturally been from various parts of the world, and presented themselves in all stages of the disease. Five of them were females.

At the time of my first examination they were classified as follows: Incipient, 46; moderately advanced, 20; far advanced, 34. Of the incipient cases, there were 28 instances of complete arrest of the disease—a percentage of 60 plus among this class. Of the second stage, 3 underwent complete arrest, a percentage of 15. No recoveries were noted in the third stage cases. The recovery rate for the entire number thus stands at 31 per cent.

Many of the cases in the second and third classes had been ill for several years before coming to Colorado. The high recovery rate in the first stage cases gives ground for the assumption that the patients first seen in the second and third stages would have vastly improved their chances by earlier climatic treatment.

The death rate stands as follows: First stage, 5; second stage, 12; third stage, 22; a percentage of 39. It must be understood that these are not at all the final figures in the series, since the results are unknown in 10 cases, which have drifted away, and in 4 others who were improving when last heard from. Further, 9 physicians are living and practising, although still presenting abundant evidence of active tuberculosis, and 7 are living, but too ill to practise. Those in the last two classes, 16 in number, are beyond the possibility, practically speaking, of recovery, and probably the unknown 10 all belong in this category. Thus, we shall not err very seriously if we state the eventual mortality as

39 (dead) plus 10 (unknown) plus 9 (living and practising, all still under observation, and all, in my opinion, hopeless so far as recovery goes) plus 7 (too ill to practise), a total of 65. The 4 improving at last accounts we shall not attempt to place.

A more cheerful light is thrown upon the statistics given, by the statement that among the 9 still living and actively practising, but with active disease, the duration has averaged about thirteen and one-half years, the extremes being five years and nineteen years. Of the 7 still living but too ill to practise, the average duration of the disease is twelve years, the extremes being three years and twenty-one years. Of the 33 cases already dead, the duration of whose disease is known, the average time was five and seven-tenth years. The extremes were less than a year in 2 cases, and twenty-five years in one case. It would appear that far less than an average proportion of cases of acute pulmonary phthisis with quickly fatal outcome has presented in this series, probably because such cases are less apt to seek climatic treatment than the more chronic forms. It is to be noted that the third stage cases, still living after many years, or who practised for many years, have been generally of the fibroid type.

The results, classified according to the age of infection, are shown in the columns below:

	18 to 25 yrs.	26 to 30 yrs.	31 to 35 yrs.	Over 36 yrs.	Total.
Recovered	10 (26.3%)	12 (38.7%)	5 (35.6%)	4 (23.5%)	31
Died	18 (47.3%)	8 (25.8%)	6 (43.0%)	7 (41.0%)	39
Living and practising	4	4	..	1	9
Living not practising	1	3	1	2	7
Improved when last heard from	1	2	1	0	4
Unknown	4	2	1	3	10
	<hr/> 38	<hr/> 31	<hr/> 14	<hr/> 17	<hr/> 100

In only 3 of the cases noted as recovering has the duration of complete arrest been less than five years, and in these 3 it is three years or over. The best prognosis is evidently found in those contracting the disease between the ages of twenty-six and thirty-five years, and the worst in those under twenty-five years.

Several instances of rapid failure and death following marriage before complete arrest of the disease were noted in the series.

I have mentioned elsewhere the danger from tuberculosis to the physicians in the natural gas regions. It is occasionally contracted or becomes suddenly active after prolonged attendance, as at confinements, in houses heated by this means far above the proper temperature, and generally but poorly ventilated. Two physicians in this series dated the origin of their trouble from the severe cold taken while driving home in a winter night after such an experience.

One physician had 200 hemorrhages in eleven years, and finally succumbed. In the early part of his disease he once drank three hundred dollars worth of whisky in seven months. Another had

more than 60 hemorrhages. One died of hemorrhage after a twenty-five-year struggle with fibroid phthisis. Another died from sudden hemorrhage after material improvement from the draining of a large cavity at the base of the lung. In 2 instances the direct cause of death was tuberculous meningitis.

No recovery was noted among the several physicians who had contracted the disease in our tropical possessions, nor have I seen recovery in any other patient whose infection originated in these regions.

I had intended to compare the results among the physicians with those among 1000 laymen taken consecutively. Because of the fact, however, that a majority of the latter were seen for purposes of diagnosis, or advice as to climatic treatment, and thus were under care for but a brief period, the records were too incomplete for use in this way. The physicians, on the other hand, have commonly kept me posted as to their condition, a large proportion being engaged in active practice in the Rocky Mountain region at the present time.

I am satisfied in my own mind that the figures presented offer strong evidence that the recovery rate among physicians coming to Colorado is a high one; that the longevity after contracting the disease is above the average; and that still better results will be obtained when yet earlier diagnosis meets with more prompt and efficient response in treatment.

I am under obligation to my associate, Dr. T. R. Love, for the tabulation of the results presented in this article.

THE HIGH CALORY DIET IN TYPHOID FEVER: A STUDY OF ONE HUNDRED AND ELEVEN CASES.

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IN 1909 Dr. P. A. Shaffer and the author¹ published the results of an investigation of the protein metabolism in typhoid fever. This investigation proved that by the use of diets of high caloric value, especially when rich in carbohydrate, it was possible to diminish, and, if the supply of carbohydrate was sufficient, to prevent the febrile loss of body protein, which on all previous diets had been so characteristic of this disease.

¹ Arch. Int. Med., 1909, iv, 538.

On the basis of this investigation a new diet was arranged for the treatment of typhoid fever. But no attempt was made in the paper referred to to discuss the therapeutic value of the diet.

A brief clinical paper² upon the subject was also published in 1909, but, in this paper, it was not possible to consider in sufficient detail either the diet or its administration.

In the four years which have elapsed since the investigation was begun, the high calory diet has been employed in the treatment of 111 cases of typhoid fever in the wards of the Second Medical Division of Bellevue Hospital. The experience derived from these cases forms the basis of the present paper. While it is my purpose to consider mainly the clinical application of the high calory diet, it will be necessary to refer from time to time to the scientific aspects of the subject.

THE DAILY FOOD REQUIREMENT. Shaffer and Coleman calculated theoretically the minimum daily food requirement of the average adult typhoid fever patient to be about 40 calories per kilogram of body weight, or approximately 3000 calories for a patient weighing 150 pounds, but their investigation showed that, in the cases studied, a mixed diet furnishing this amount of energy was not sufficient to establish nitrogen equilibrium. The best results in the maintenance of nitrogen equilibrium were obtained with diets furnishing from 60 to 80 calories per kilogram per day, or from 4000 to 5500 total calories. The optimum requirement, however, varied greatly in different cases and at different stages of the disease, but was always greater than the calculated minimum.

Grafe³ found recently, in a study of the total metabolism of 12 cases of typhoid fever in the fasting state, that the heat production amounted only once to 40 calories per kilogram (the total in this instance being 1740), and never exceeded 2798 calories a day.

While the discrepancy in these results is accentuated by the fact that Grafe's patients were fasting, it cannot, with our present knowledge, be explained. But, on the basis of clinical experience and of our own laboratory results, I believe, and for the purposes of this discussion shall assume, that the more nearly nitrogen equilibrium is attained—in other words, the more perfectly nutrition is maintained—the greater are the chances in the patient's favor. Accordingly, I shall place the daily requirement of the average adult typhoid fever patient at more than 40 calories per kilogram, but would emphasize the statement that the optimum amount of food can be determined only by the needs of each patient individually.

Patients of small stature, including children, require more energy per kilogram, but not necessarily more actual energy, than average adults, because of the disproportion of surface area to weight.

² Coleman, *Jour. Amer. Med. Assoc.*, 1909, liii, 1145.

³ *Deutsch. Arch. f. klin. Med.*, 1910, ci, 209.

THE PROTEIN, FAT, AND CARBOHYDRATE RATIOS. The next question requiring consideration is the relative proportions of protein, fat, and carbohydrate which should enter into the diet of the typhoid fever patient. So little is known concerning metabolism in typhoid fever that a full discussion of the ratios would of necessity be largely theoretical, and therefore unsuited to a paper of this character.⁴

Protein. The best results in the sparing of body protein obtained by Shaffer and Coleman were with diets containing from 10 to 15 grams of nitrogen, or 62 to 94 grams of protein, a day. Since Grafe essentially confirms these results, this quantity may be accepted provisionally as the optimum protein ration. But it is not improbable that the requirement varies in different stages of the disease, and that even in cases where nitrogen equilibrium has been maintained during the febrile period, there may be an increased demand for nitrogen during convalescence to repair the damage inflicted upon the tissues by the endotoxin.

Gelatin. Tissue protein cannot be built up from gelatin; therefore gelatin alone cannot supply the nitrogen needs of the body. But Murlin⁵ has shown that two-thirds of the minimum daily protein ration may be replaced by gelatin, provided the carbohydrate supply is sufficient, without detriment to health.

While I have used gelatin only to a limited extent, there is no apparent reason why it may not be permitted as a part of the diet for the sake of variety.

Fat. We possess very little knowledge of the fat requirement in typhoid fever. But physiological economy would appear to make it expedient in fever, as in health, that a portion of the energy of the food should be supplied in the form of fat. Clinical evidence indicates that the fat needs of the typhoid fever patient vary in different stages of the disease. Many, if not the majority of patients, are able to take more fat in the steep-curve period and in convalescence than in the earlier stages of the disease. Fat has often furnished in these periods one-half of the total energy of the food of the cases in the present series, and the patients have appeared to be the better for it.

Carbohydrate. Of the three classes of foodstuffs, carbohydrate plays by far the most important part in preventing the consumption of the body tissues in fever. Grafe's studies on the total metabolism of fasting typhoid fever patients agree with the results of Shaffer and Coleman in establishing this fact. It has been found that the amount of carbohydrate necessary to protect the body protein varies in different subjects and at different stages of

⁴ Certain phases of metabolism in this disease are now under investigation with the aid of the Benedict respiration apparatus.

⁵ Amer. Jour. Phys., 1907, xix, 285.

the disease, therefore only a general recommendation can be made for clinical purposes; that the greater portion of the energy of the diet should be supplied in the form of carbohydrate, unless there is some definite indication to the contrary. A number of patients in this series have taken from 30 to 60 carbohydrate calories per kilogram per day.

PREVIOUS DIETS. While it will not be possible to discuss at length the different diets which have been employed in the treatment of typhoid fever, a brief summary of them may be given. Three types of diet have been used: (1) The meat-broth-carbohydrate-water diet of Graves, which furnished, at the most liberal estimate, not more than 300 calories a day; (2) the milk diet, from which the patient receives about 1300 calories a day, assuming that he takes two quarts; and (3) the so-called liberal diets. These diets furnish at most only about 2000 calories a day. They were constructed upon empirical data, and, as might be expected, are open to criticism. More attention has been devoted to increasing the variety of foods allowed than to the dynamic value of the diet as a whole. Likewise, undue emphasis has been placed upon the necessity of increasing the protein.

The history of the typhoid diets thus indicates a definite though gradual tendency to raise the energy value of the food. The change from Graves' diet to milk added approximately 1000 calories a day to the patient's dietary; the change from milk to the liberal diets added about 700 more. But according to the results of Shaffer and Coleman, the most generous of these diets falls short of the patient's needs by about 1500 to 2000 calories a day.

THE SELECTION OF THE DIET. The most important considerations governing the selection of foods for the typhoid fever patient are their digestibility, absence of harmful residue, fuel value, and palatability.

Protein Foods. The choice of protein foods lies among the meats, eggs, milk, and the proteins contained in the carbohydrate foods.

Meats. The objections which may be brought against meat and preparations of meat raise the question whether they should be given at all to patients suffering from typhoid fever. Meats differ so much in digestibility, according to variety, "cut," method of cooking, etc., that it is difficult to make a comprehensive statement regarding them. Some meats are relatively indigestible in health; others appear to be digested readily even in disease. Probably the majority of physicians believe that patients suffering from febrile diseases are better off without meat. When meats are allowed to fever patients, there is likely to be an excess of protein in the diet, and Ewing and Wolf⁶ have shown that a relative excess

⁶ Arch. Int. Med., 1909, iv, 330.

of protein may cause serious disorders of metabolism in severe cases of typhoid fever, especially if the patients are undernourished. Furthermore, the products of the putrefaction of meat in the intestine may not only give rise to digestive disorders, but may irritate the kidneys during their excretion and produce albuminuria. Meat extracts, such as beef juice and bouillon, have often been recommended, and sometimes have constituted the sole article of the typhoid diet. While the use of small quantities of these preparations may be advantageous at times to stimulate the appetite, two objections may be raised to them—the small amount of energy they furnish and the high percentage of extractives they contain. Beef juice as ordinarily prepared furnishes 25 calories to each 100 c.c. (3 ounces); bouillon furnishes only 8. The extractives in beef juice and in bouillon average about 2 per cent. Beyond stimulating the appetite, they serve no useful purpose, and may prove toxic.

Since meat and meat preparations are not necessary in order to supply the typhoid fever patient with nitrogen, the objections which have been raised to them render it advisable that they be excluded from the diet or at least that they be given with caution.

Eggs. Egg albumin water has been used extensively in the treatment of typhoid fever. White of egg, shaken up with ice, flavored with lemon or sherry and sugar, and strained, has also been recommended. But the value of whole eggs has apparently been overlooked, though they have been employed extensively in other febrile diseases, as, for example, in septic diseases and tuberculosis. Aufrecht and Simon⁷ have shown that lightly boiled and raw eggs have a higher food value as part of a mixed diet than a corresponding amount of meat, and that lightly boiled eggs are slightly more digestible than raw eggs. The digestibility of boiled eggs is somewhat lowered by the addition of butter.

Patients with typhoid fever take readily and digest from four to six eggs a day. Eggs may be used to supply not only nitrogen, but energy. Six eggs, for example, furnish about 7 grams of nitrogen and 480 calories.

Fats. The most suitable forms of fat for the typhoid fever diet are cream, butter, and yolk of egg. The principal objections to fat are that it may cause nausea, vomiting, other digestive disturbances, and diarrhea. I shall not enter here into a discussion of the disputed question whether fat is capable of causing disturbances of metabolism. It will only be necessary to say that there has been no evidence in any of the cases of this series of such disturbances, though many of them took large amounts of fat.

The tolerance for fat in typhoid fever is much greater than has been supposed. I have often given as much as 200 to 250 grams

⁷ Deutsch med. Woch., 1908, xxxiv, 2308.

of fat a day without producing disturbances of any kind. Yet fat has shown a tendency to cause nausea and vomiting and diarrhea when the quantity has been carried too high. These symptoms, however, have always subsided promptly when the fat was diminished or stopped. Patients differ in their behavior toward fat, and the fat tolerance must be determined in each case.

Milk. Milk has been used probably more than any other food in the treatment of typhoid fever, yet few subjects provoke more discussion in medical assemblages than the value of milk in this disease. Many persons declare they cannot take milk even in health. Many physicians believe that milk always produces digestive disturbances and tympanites in typhoid fever. The majority of typhoid fever patients taking the milk diet grow very tired of it before they are permitted to have other food. This, however, is an argument not so much against milk as against the practice of limiting the patient to one article of food.

Milk is an important, but not essential, constituent of the high calory diet. Because of its importance, the value of milk and the arguments against it must be considered at some length. Van Noorden⁸ states that the idea which many people have that they cannot take milk is "purely imagination; . . . there are almost no people who do not bear milk well or who cannot accustom themselves to its use." Peabody,⁹ in an article protesting against milk as an exclusive diet in typhoid fever, says: "Milk will always remain the most serviceable general food in disease, and especially in fever, largely because it is swallowed with much less effort than attends the taking of other foods . . . and because it is so commonly well borne." Pavlov¹⁰ states that "milk causes a secretion both from the stomach and pancreas; . . . milk excites not only a really effective, but also a very economic secretion; . . . a much larger fraction of its nitrogen is free for use by the organism than with any other kind of food. How admirably, therefore, the food prepared by nature subserves its purpose when compared with all others."

In rare instances, however, persons exhibit a definite idiosyncrasy against milk. Halberstadt¹¹ considers the idiosyncrasy to be a symptom of a congenital constitutional anomaly, comparable to anaphylaxis. The idiosyncrasy may be against the albumin, fat, or whey. In some instances the deleterious effects of milk are thought to be due to a change it causes in the flora of the intestine. Definite poisoning occurs in these cases, often with inflammatory changes in the alimentary tract, and they must not be confounded with patients in whom, it is claimed, digestive disturbances and

⁸ Twentieth Century Practice, vol. ii, p. 153.

⁹ New York Med. Record, 1892, xlii, 620.

¹⁰ The Work of the Digestive Glands, 2d English edition, 1910, p. 229.

¹¹ Arch. f. Kinderheilk., 1911, lv.

tympanites occur from the use of milk. Tugendreich¹² has described a similar poisoning by buttermilk under the title of "buttermilk fever."

With regard to the statement that milk always produces digestive disturbances and tympanites in typhoid fever, each physician will probably be guided by his own experience. There is no inherent reason why milk should be more indigestible in typhoid than in any other fever. My experience is in favor of milk. For years before the development of the high calory diet I gave milk exclusively to patients suffering from the disease. Since 1907 milk has formed an important part of the diet. Yet it is a familiar fact that there is a limit to the quantity of milk which patients can digest. When this limit is overstepped, the bulk of the stools increases, milk curds appear, and diarrhea and tympanites may occur. But, to say that a patient cannot take milk because excessive quantities cause alimentary disturbances is not a well-considered argument. In addition to the fear of causing such disturbances, excessive quantities should be avoided, for the reason that the total potential energy of the milk is not utilized, as is shown by the waste in the stools.

What quantity of milk is to be considered excessive can be determined only by the ability of the individual patient to digest it. This ability probably varies under different conditions. In my experience the average patient with typhoid fever is able to digest $1\frac{1}{2}$ to 2 quarts of milk a day without difficulty.

The argument that milk favors the growth of the typhoid bacillus in the intestine is largely theoretical, and is based upon the discarded conception that typhoid fever is an intestinal disease.

While milk is not an essential constituent of the high calory diet—no one article of food is—it will be found difficult to supply a patient with sufficient energy on a milk-free diet without unduly disturbing the protein, fat, and carbohydrate ratios. But after all has been said, the quantity of milk in the diet must be arranged according to the tolerance of the patient for it. If it is known to produce digestive disturbances, it should be peptonized, or the quantity be diminished, or it should be stopped altogether.

Carbohydrates. The carbohydrate supply may be obtained from the starches or sugars, or both.

Starches. Only such starchy foods should be selected as are easily digested and contain no cellulose. Foods with a low percentage of water are to be preferred, as otherwise their bulk is objectionable. Crackers and toast are especially valuable. Well-boiled cereals (without cellulose), rice, and baked or mashed potato may be given in moderation for sake of variety. The only objection to starchy foods in typhoid fever is their bulk.

¹² Deutsch. med. Woch., 1909, xxxv², 2319.

Sugars. In order to meet the carbohydrate demands of the patient, one or more of the sugars must be employed. For practical reasons the choice lies between cane-sugar, lactose, and glucose. Cane-sugar is so sweet that it soon palls upon the taste when given in quantity. Opinions differ as to whether it ferments readily in the intestine. Jacobi¹³ states that it ferments less easily than lactose in the case of children. Adults probably differ in their ability to handle it. I have given a tablespoonful at a time in coffee, lemonade, etc., and should not hesitate to increase this amount cautiously. Glucose, because of its taste, likewise soon palls upon the senses. It has not been given to any of the cases of this series.

An impression prevails that lactose does not ferment readily in the intestine, though I have not been able to find the investigations upon which this opinion rests. The typhoid bacillus is not capable of fermenting lactose. In my experience it is not fermented readily in typhoid fever by other organisms than the typhoid bacillus, nor has it exhibited the laxative properties which have been attributed to it. Lactose is not very sweet and does not pall quickly upon the taste. Halasz¹⁴ found that persons in health are able to take 150 grams of lactose at a time without the production of glycosuria, while persons suffering from dilatation or tumors of the stomach were able to take only 120 grams. Bauer¹⁵ found the tolerance for lactose in cirrhosis of the liver to be 80 to 100 grams. I have never given more than 140 grams at a time. In no case of the series, whose urine was examined repeatedly (the urine of about 25 of the cases was examined daily), did glycosuria occur.

It should be added that Längstein¹⁶ is of the opinion that lactose, of all the carbohydrates, is least adapted to the child whose nutrition is disturbed, and that cane-sugar is more valuable. Howland tells me that he has found it difficult to give the high calory diet, as here outlined, to young children. Kerr,¹⁷ on the other hand, recommends the diet. As no patient of this series was under twelve years of age, I have formed no opinion.

Fruits. Lemonade, orange juice and orangeade, and apple-sauce have been given to many patients of this series. There has been no reason to think that these fruits have disagreed with them. Fruit has not been permitted, however, or has been given in small quantity and with caution, when patients were suffering from diarrhea.

The foods which have been mentioned above are the only ones which have been employed to a sufficient extent to justify their

¹³ Personal communication.

¹⁵ Wien. med. Woch., 1906, lvi, 20, 2537.

¹⁶ Jour. Amer. Med. Assoc. (Berlin letter), 1910, lv, 1823.

¹⁷ Amer. Jour. Obstetrics, 1909, lx, 1064.

¹⁴ Deutsch. med. Woch., 1908, xxxiv, 818.

recommendation, but the diet will unquestionably admit of further elaboration, especially in the matter of variety.

Proprietary Foods. A great variety of proprietary foods are manufactured. They may be roughly classified as meat extracts, other protein foods, some of which have been partially predigested, and foods which have been reënforced by the addition of carbohydrate or fat, or both. They are marketed as liquids, pastes, and powders. The protein foods are made from meat, eggs, milk, blood, plants, malt, and of mixtures of these. The sources of these foods suggest that their native ingredients may be equally valuable.

Concerning meat extracts, Bigelow and Cook¹⁸ state that "meat juice prepared in the home or hospital . . . is far superior as a food to the commercial meat extracts and so-called meat juices." Many of the liquid preparations contain alcohol—some as much as 20 per cent.—which fact must be borne in mind or an excessive quantity of this drug may be administered. The so-called predigested protein foods must likewise be given with caution, since it has been shown that proteoses and peptones may cause diarrhea and other digestive disorders. The work of Ewing and Wolf, as already mentioned, has demonstrated the danger of giving protein to patients who take other foods poorly, and the frequently advertised advice to give such patients proprietary protein foods must be unreservedly condemned.

Lusk¹⁹ states that "the principal value of 'patent' foods lies in their flavor. . . . That beef, milk, cream, butter, and rice are equally suitable for all the purposes of proper living is a fact not sufficiently advertised."

If it should become necessary in any case of typhoid fever to give a patient an artificial food, a preparation in which carbohydrate predominates should be selected, and its fuel value should be clearly understood.

In my experience proprietary foods are unnecessary in the treatment of typhoid fever. I have always found that, if a patient could take food at all, he could take a natural food.

ARGUMENT FOR THE HIGH CALORY DIET. The value of the high calory diet must rest ultimately upon the results obtained from its use in a large number of cases. Pending this verdict, estimates of its value may be made from such sources as are available. These sources comprise our knowledge of nutrition, of bacterial infections in general, and the opinions of physicians of experience in the treatment of typhoid fever.

It is axiomatic that life cannot continue unless the body is supplied with energy for its metabolic exchanges. If food is not available in sufficient quantity, the tissues of the body will be

¹⁸ United States Dept. Agriculture Bull., No. 114, 1908.

¹⁹ The Science of Nutrition, first edition, p. 119.

drawn upon. Clinical evidence as well as numerous experimental investigations have shown this to be true in fever as well as in health. There is probably no infective disease, except those which affect the alimentary tract locally, which is benefited by partial or complete starvation.

Though typhoid fever often strikes down persons in apparently perfect health, it is generally accepted as true that both the lower animals and men who are undernourished are less able to resist bacterial invasion. Furthermore, healthy laboratory animals furnish a better immune serum than those which are sickly, and the belief prevails that patients suffering from many, if not all, infective diseases are more likely to recover when properly nourished. When in addition we consider that, as Grafe has shown, metabolism in typhoid fever probably follows normal laws, there is no known reason why patients suffering from this disease should be partially starved. On the contrary, and especially in view of the increased metabolism in fevers, all indications point to the desirability, if not necessity, of supplying patients with all the food they require.

Physicians who have raised the nutritive values of their diets are practically unanimous in their opinions as to the beneficial effects of the change. Graves²⁰ believed that even his meagre diet modified favorably the course of the disease as he knew it. Trousseau²¹ shared this belief. In advocating the milk diet, Flint²² compared the typhoid fever patient to a person in danger of drowning, and said: "As a person in this situation requires only to be buoyed up by some support, so the fever patient in a similar emergency may need only supporting means to live until the disease ends."

Marsden²³ claimed that his patients recovered more rapidly, and that the tendency to asthenic complications was lessened.

Barrs²⁴ thinks that the sooner a patient returns to a natural diet the sooner will his nutrition be such as to place his intestine under the best possible condition for healing; that free feeding is likely to modify favorably the death rate, to shorten convalescence, and to diminish the risks of complications and sequelæ.

Kinnicutt²⁵ found, in an analysis of 600 cases on liberal diets, that hemorrhage and perforation were less frequent than on a restricted diet, chiefly milk, and that relapses were not increased.

Many other favorable opinions could be cited, but it seems unnecessary. It is a significant fact that the adverse criticisms of the liberal diets have come for the most part from physicians who have not employed them. Few or no physicians who have given these diets an extended trial have returned to the older restricted methods of feeding. If one accepts the foregoing evidence, the

²⁰ Clinical Medicine, New Sydenham Society, 1884, i, 136.

²¹ Clinique Médicale, 4th ed., i, 350.

²² London Lancet, 1900, i, 90.

²³ Bost. Med. and Surg. Jour., 1906, clv, i.

²⁴ Pract. of Med., 6th ed., p. 982.

²⁵ Brit. Med. Jour., 1897, i, 125.

high calory diet is deprived of the radicalism which has been attributed to it, the object of the diet being simply to supply patients with all the food they need, instead of supplying them with part of it.

CRITICISMS OF THE HIGH CALORY DIET. The only criticisms which have been made of the high calory diet, so far as I am aware, relate to the ability of the patient to digest and absorb the amount of food recommended.

Von Hoesslin²⁶ proved that digestion in typhoid fever is only slightly below normal, not more than 10 to 15 per cent.

Eugene F. Du Bois has investigated during the last year the food losses in the stools of several cases of this series. The results will be published in full by him later on, but a brief summary of them may be given here.

The protein losses, with patients taking from 65 to 118 grams, were usually under 10 per cent. The loss in a normal man on the same diet, studied as a control, was 7.9 per cent.

The fat loss in the second week of the disease, when the temperature was high, with patients taking from 147 to 200 grams, averaged 8.84 per cent. The loss in the steep-curve period of the third and fourth weeks, with the patients taking from 150 to 258 grams daily, was 4.15 per cent. The fat loss in the control, taking 164 grams daily, was 2 per cent. According to Rubner, a normal man taking 79.9 grams of fat a day in milk lost 7.1 per cent. in the stools, and a normal man taking 214 grams of fat in the form of butter lost 2.7 per cent.

The carbohydrate loss in all periods of the disease, with patients taking from 215 to 567 grams daily, was only 0.1 to 0.3 per cent. The loss in the control while taking 249 grams was 0.1 per cent.

The results obtained by Du Bois demonstrate that the ability of the typhoid fever patient to digest and absorb the high calory diet is remarkable, and they may be interpreted as an additional indication of the patient's need for such surprisingly large amounts of food. These results should not be interpreted to mean, however, that the typhoid fever patient may be fed indiscriminately with foods which may be taken by the healthy man with impunity, but simply that carefully selected, easily digested foods may be given to typhoid fever patients (in quantities proportioned to the ability of the patients to digest them) without fear of harm.

The further fact should be noted (and this has been observed by all persons who have been brought in contact with the patients), that the stools of patients on the high calory diet presented an unusually normal appearance.

ADMINISTRATION OF THE DIET. A false impression exists concerning the high calory diet, namely, that a patient should be

²⁶ Virchow's Archiv, 1882, lxxxix.

given large amounts of food, especially milk sugar, simply because he has typhoid fever, irrespective of the result produced. The physician should endeavor to maintain nutrition in all cases, but I would emphasize the statement that *no patient should be given more food than he is capable of digesting and absorbing*. If the food is vomited or passes through the intestine unabsorbed, the very object of the diet, improvement of the patient's nutrition, is defeated.

In no case can we do more than attempt to give patients the amount of food they require. Failure to accomplish this may depend either upon lack of proper attention to detail on the part of the physician or to lack of coöperation on the part of the nurse, as well as to obstacles which the disease itself interposes. The physician should possess at least a rudimentary knowledge of the calory values of foods. But probably the chief requisite to the successful administration of the diet is intelligent coöperation on the part of the nurse. When a nurse is trained in the use of the diet, general directions regarding the total number of calories and the protein, fat, and carbohydrate ratios will suffice. At her discretion she will increase or diminish the total amount of food, or of particular articles, until further instructions. When a nurse is not trained in the use of the diet, the physician himself must assume immediate control of the feeding.

Cautions in Giving the Diet. Whenever the administration of the high calory diet is undertaken, careful attention should be paid to the behavior of the stomach, the condition of the abdomen, and the number and character of the stools. If any article of food causes persistent disturbances of digestion, it should be diminished in quantity or stopped. The qualification "persistent" is made because neither occasional vomiting, slight tympanites, or mild diarrhea has been found to be a contraindication to the diet.

One should proceed cautiously in all cases in increasing the amount of food, but not necessarily slowly. If for any reason a patient takes all food poorly, as in cases with alcoholic or other gastritis, the diet should be reduced to the simplest terms, but the patient should be given all the food he can take. For reasons already stated, such patients should not be fed exclusively upon meat broths or other preparations in which protein predominates. Attention should be directed to the fact that it is not uncommon for patients on the high calory diet to have several formed stools a day. This, of course, is not an indication to modify the diet. Many patients who, while taking the high calory diet, have only one stool a day will have from three to six stools a day when put upon the "regular" hospital diet containing meat and vegetables.

Milk sugar may cause nausea and vomiting, especially at first, if the quantity is increased too rapidly. I have found, however, only a limited number of patients whose stomachs could not be

educated to tolerate it, even in large quantities. When milk sugar causes nausea or occasional vomiting, it is necessary to diminish the quantity or to change the method of its administration. If it causes persistent nausea and vomiting, it should be stopped, but may be begun again in a day or two in smaller amounts. The addition of only a teaspoonful to milk or other suitable articles of food is just so much energy gained. A similar course should be pursued if the milk sugar causes tympanites, though at times, when this has been slight, I have diminished but not stopped it.

Cream may cause gastric disturbances or diarrhea. In the former case it should be stopped; in the latter, diminution of the quantity may be sufficient to bring the diarrhea under control. I have not considered it necessary to modify the diet when patients were having only two or three diarrheal stools a day. Not infrequently patients entering the hospital with diarrhea have had this stop under the cautious administration of the diet.

The Amount of Food. As has already been pointed out, the amount of food which a patient requires must be determined by *his individual needs*. The calculated requirement serves only as a general indication of them. The condition of the patients of this series, in whom the nitrogen balance was determined, corresponded in general with the amount of nitrogen lost. Patients losing nitrogen lost weight, and the more nearly nitrogen equilibrium could be maintained, the better was the condition of the patient. But since it is manifestly impossible to determine the nitrogen balance, except in a few cases, clinical guides to the patients' needs must be sought. Two such guides have been found useful—the *weight* of the patient, and the state of his *appetite*. It is not practicable to weigh patients in private practice, and the physician must depend upon his judgment to tell whether a patient is gaining or losing in weight. A patient who is losing weight is evidently drawing upon his own tissues, and certainly requires more food.

If hunger has any significance, we must believe that it indicates the need of food. I always try to appease the appetite of a patient who is hungry.

In the earlier stages of the disease, when the temperature is continuously high, it is always difficult and sometimes impossible to give patients the amount of food they require, that is, the amount which will prevent loss of weight. In perhaps the majority of severe cases it will not be possible to give more than 3000 calories, but as the temperature passes into the steep-curve period, the number of calories may gradually be increased. In this period and in convalescence patients take eagerly from 4000 to 6000 calories a day (one patient took 7400 calories). The question of the advisability of permitting patients to have such large amounts

of food has been raised by physicians and others who have seen the cases. In every instance these quantities have been reached only in response to requests from the patients for more food. Some patients have complained of hunger while taking 3500 to 4000, and even more, calories a day, and I have seen no reason for attempting to curb their appetites. It is not likely that all this food is used for producing energy. Part of it is probably stored as glycogen and fat. As will be pointed out later, gains of a pound a day in weight are not uncommon in the steep-curve period and in convalescence. If only half of such a gain is represented by fat, approximately 2000 of the calories would be accounted for, leaving not much more of the potential energy of the diet than is generally conceded to be necessary for the daily expenditures of the patient. Not infrequently patients who have lost flesh during the more active stages of the disease will regain their weight before the temperature reaches normal.

The question of what weight we shall permit the patient to reach presents itself during convalescence in nearly all cases. I have no definite opinion to express upon this question, but because of the after-tendency to obesity in many instances, I have usually followed the practice of changing or limiting the patient's food when the normal weight has been attained. So far as my information goes, the high calory diet does not predispose to obesity after the fever.

Details of Administration. The successful administration of the high calory diet depends upon unremitting attention to detail. It is a good plan to make a frank statement to the patient regarding the object of the diet whenever, in the opinion of the physician, this can be done. However, it is not always wise to enter too fully into particulars. Very often I tell patients that the more they eat, the sooner they will get well, and the effect of the suggestion upon the quantity of food which they will take is sometimes surprising. I tell every patient who is capable of appreciating the advice, to ask the nurse for more food if he wants it, and I tell the nurse to give the patient all the food he can digest and absorb.

Typhoid fever patients cannot all be fed alike. Their preferences for and idiosyncrasies to foods are not removed by the fever. Yet often the judicious substitution of one article of food or dish for another will increase the fuel value of the diet by several hundred calories. Sometimes patients who complain that the milk is too sweet when it contains one-half to one ounce of milk sugar will take eagerly from two to four ounces of milk sugar in custard, ice cream, or lemonade. As in every other illness, the physician should permit as great variety of foods as is consistent with the patient's wellbeing.

Ordinarily, when a patient first comes under observation he is put upon plain milk for a day or two. The subsequent procedure

depends upon the patient's condition; that is, whether he is suffering from a mild or severe attack of the disease. In the former case he may be allowed foods which require mastication; in the latter, the diet should be liquid.

FOODS AND THEIR CALORY VALUES.²⁷ All of the foods and recipes which follow have been given thorough trial, and are recommended with confidence for appropriate cases.

Name.	Amount.	Calories.
Apple sauce	1 ounce	30
Bread	Average slice (33 grams)	80
Butter	1 pat ($\frac{1}{2}$ ounce)	80
Cereal (cooked)	1 heaping tablespoonful ($1\frac{1}{2}$ ounces)	50
Crackers	1 ounce	114
Cream (20 per cent.)	1 ounce	60
Egg	1 (2 ounces)	80
Egg, white	1	30
Egg, yolk	1	50
Lactose	1 tablespoonful (9 grams)	36
Milk (whole)	(1 pint 350) 1 ounce	20
Potato (whole)	1 medium	90
Potato (mashed)	1 tablespoonful	70
Rice (boiled)	1 tablespoonful	60
Sugar, cane	1 lump	16
Sugar, milk ²⁸	1 tablespoonful (9 grams)	36
Toast	Average slice	80

Rubner's figures for calculating the calory values of the different foodstuffs will be found useful: 1 gram pure protein furnishes 4.1 calories; 1 gram pure carbohydrate furnishes 4.1 calories; 1 gram pure fat furnishes 9.3 calories. Nitrogen multiplied by 6.25 equals protein.

FOOD COMBINATIONS AND RECIPES. For the convenience of those desiring to use the high calory diet, the following combinations of foods are given. They are most useful in the early stages of the disease, or in the case of patients who are unable to take solid food.

For 1000 calories a day:	Calories.
Milk, 1 quart (1000 c.c.)	700
Cream, $1\frac{2}{3}$ ounces (50 c.c.)	100
Lactose, $1\frac{2}{3}$ ounces (50 grains)	200
This furnishes 8 feedings, each containing:	
Milk, 4 ounces	80
Cream, 2 drams	15
Lactose, 6 grams	24

²⁷ The calory values given in the table are approximate, for the most part, but are sufficiently accurate for practical purposes. The values stated are based upon the tables of Atwater and Bryant, Schall and Heisler, Arnold's Diet Charts, and upon weights taken in the hospital.

²⁸ For practical purposes, the milk sugar may be measured in a medicine glass. Each measured ounce equals 18 grams in weight. If milk sugar is added to water in the proportion of 24 grams to 30 c.c. and the water brought to the boiling point, the milk sugar is completely dissolved. Such a solution, made daily or just before use, will be found convenient in administering the diet.

		Calories.
For 1500 calories a day:		
Milk, $1\frac{1}{2}$ quarts (1500 c.c.)		1000
Cream, $1\frac{2}{3}$ ounces		100
Lactose, $3\frac{1}{3}$ ounces (100 grams)		400
This furnishes 6 feedings, each containing:		
Milk, 8 ounces		160
Cream, 2 drams		15
Lactose, 16 grams		64
For 2000 calories a day:		
Milk, $1\frac{1}{2}$ quarts		1000
Cream, 8 ounces (240 c.c.)		500
Lactose, 4 ounces (125 grams)		500
This furnishes 7 feedings, each containing:		
Milk, 7 ounces		140
Cream, 1 ounce		60
Lactose, 18 grams		72
For 2500 calories a day:		
Milk, $1\frac{1}{2}$ quarts		1000
Cream, 8 ounces		500
Lactose, 8 ounces (250 grams)		1000
This furnishes 7 feedings, each containing:		
Milk, 7 ounces		140
Cream, 1 ounce		60
Lactose, 36 grams ²⁹		144
For 3000 calories a day:		
Milk, $1\frac{1}{2}$ quarts		1000
Cream, 1 pint (480 c.c.)		1000
Lactose, 8 ounces		1000
This furnishes 8 feedings, each containing:		
Milk, 6 ounces		120
Cream, 2 ounces		120
Lactose, 1 ounce (30 grams)		120
For 3900 calories a day:		
Milk, $1\frac{1}{2}$ quarts		1000
Cream, 1 pint		1000
Lactose, 16 ounces (480 grams)		1900
This furnishes 8 feedings, each containing:		
Milk, 6 ounces		120
Cream, 2 ounces		120
Lactose, 2 ounces		240

When the above combinations are employed, it is generally desirable to add eggs to the diet in order to raise the nitrogen to the desired amount. The eggs may be soft-boiled or be shaken up in any of the above feedings unless distasteful to the patient, though the addition of an egg makes the stronger mixtures very rich. I have given some patients who seemed unable to get enough to eat 4 ounces of milk, 4 ounces of cream, 2 ounces of milk sugar, and an egg at a feeding. Such patients, however, are exceptional.

Milk toast, with the addition of butter or cream, is relished by many patients.

The following menus were arranged by Miss Mary E. Sheehan, head nurse in Ward A1 of Bellevue Hospital, and have been em-

²⁹ If this and the following combinations are too sweet, a portion of the milk-sugar may be given in some other form.

ployed, with such modifications as individual patients required, for the last two years. They may be followed in general at any stage of the disease if the patient is capable of taking solid and semisolid food, and if he is hungry, but are most useful in the later stages, and in convalescence. The night feedings are given when the patients' temperatures are taken in the course of the ward routine.

The diet for this day furnishes 3910 calories.

	Hours.	Total.	Calories.
Milk, 6 ounces	9 A.M.; 1, 3, 7	1260 c.e.	860
Cream, 2 ounces	10 P.M.; 1, 4	420 c.e.	840
Lactose, 10 grams		70 grams	280
			<hr/> 1980
At 11 A.M.	Calories.	At 5 P.M.	Calories.
Egg, 1	80	Egg, 1	80
Mashed potota, 20 grams	20	Cereal, 3 tablespoonfuls	150
Custard, 4 ounces	250	Cream, 2 ounces	120
Toast (or bread), 1 slice	80	Applesauce, 1 ounce	30
Butter, 20 grams	150	Tea.	
Coffee.		Cream, 3 ounces	180
Cream, 2 ounces	120	Lactose, 20 grams	80
Lactose, 20 grams	80		<hr/> 640
	<hr/> 780		

At 7 A.M.	Calories.
Egg, 1	80
Toast, 1 slice	80
Butter, 20 grams	150
Coffee.	
Cream, 2 ounces	120
Lactose, 20 grams	80
	<hr/> 510

Milk sugar lemonade may be substituted for the milk mixture at three o'clock.

The diet for this day furnishes 5580 calories.

	Hours.	Total.	Calories.
Milk, 5 ounces	9 A.M.; 11, 1, 3, 7	1200 c.e.	820
Cream, 2 ounces	10 P.M.; 1, 4	720 c.e.	1440
Lactose, 15 grams		120 grams	480
			<hr/> 2740
At 11 A.M.	Calories.	At 5 P.M.	Calories.
Eggs, 2	160	Egg, 1	80
Toast, 2 slices	160	Toast, 2 slices	160
Butter, 20 grams	150	Butter, 20 grams	150
Mashed potato, 70 grams	70	Cereal, 6 tablespoonfuls	290
Custard, 8 ounces	500	Cream, 4 ounces	240
	<hr/> 1040	Applesauce, 1 ounce	30
		Tea.	
		Cream, 2 ounces	120
		Lactose, 20 grams	80
			<hr/> 1150

At 7 A.M.	Calories.
Egg, 1	80
Toast, 2 slices	160
Butter, 20 grams	150
Coffee.	
Cream, 3 ounces	180
Lactose, 20 grams	80
	<hr/>
	650

The diet for this day furnishes 5570 calories. The ménu for the hospital "dinner" calls for chicken, and therefore should not be employed until convalescence is well advanced.

	Hours.	Total.	Calories.
Milk, 5 ounces	9 A.M.; 11, 1, 7	1050 c.c.	700
Cream, 3 ounces	10 P.M.; 1, 4	630 c.c.	1260
Lactose, 15 grams		105 grams	420
			<hr/>
			2380

At 11 A.M.	Calories.	At 5 P.M.	Calories.
Eggs, 2	160	Toast, 2 slices	160
Mashed potato, 80 grams	80	Cereal, 6 tablespoonfuls	290
Custard, 8 ounces	500	Cream, 2 ounces	120
Creamed chicken, 1 ounce	50	Lactose, 20 grams	80
Toast, 2 slices	160		<hr/>
Butter, 20 grams	150		650
	<hr/>		
	1100		

At 3 P.M.	Calories.
Lemonade (lactose, 120 grams)	480

At 7 P.M.	Calories.
Egg, 1	80
Cereal, 5 tablespoonfuls	250
Cream, 2 ounces	120
Toast, 2 slices	160
Butter, 20 grams	150
Coffee.	
Cream, 2 ounces	120
Lactose, 20 grams	80
	<hr/>
	960

The following recipes were arranged by Miss Edna Cutler, formerly Dietitian to Bellevue Hospital. They were arranged with the double purpose of adding variety to the patient's dietary, and rendering the milk sugar more palatable, thus making it possible to increase the quantity administered. I have tasted most of these dishes, and have found them savory. Any of them may be given to suitable patients at appropriate times.

Cocoa with milk:	Calories.
1 rounding teaspoonful of cocoa	50
2 ounces of milk sugar	240
4 ounces of milk	80
2 ounces of cream	120
	<hr/>
	490

Mix the sugar and cocoa; cook in the milk until dissolved. Serve with the cream.

Cocoa:	Calories.
1 heaping teaspoonful of cocoa	50
2 ounces of milk sugar	240
$\frac{1}{2}$ cup of water.	
3 ounces of cream	180
	<hr/> 470

Mix the cocoa and sugar, add the water, and boil. Then add the cream, or use less cream and serve with whipped cream.

Coffee:	Calories.
$1\frac{1}{2}$ ounces of milk sugar ³⁰	180
4 to 5 ounces of strong coffee.	
2 ounces of cream	120
	<hr/> 300

Plain junket or rennet custard:	Calories.
25 grams (—1 ounce) of milk sugar	100
5 ounces of milk	100
$\frac{1}{4}$ junket tablet.	
1 ounce of cold water.	
Few drops of vanilla.	
	<hr/> 200

See directions for cocoa junket.

Cocoa junket:	Calories.
1 teaspoonful of cocoa	50
25 grams of milk sugar	100
5 ounces of milk	100
$\frac{1}{4}$ junket tablet dissolved in 1 ounce of cold water.	
	<hr/> 250

Mix the cocoa and sugar, add the milk, and heat *lukewarm*, stirring constantly; add the dissolved junket, stir thoroughly, and leave in a cool place to set.

Soft custard:	Calories.
1 cup of milk (8 ounces)	160
1 egg	80
2 ounces of milk sugar	240
Speck of salt.	
2 to 3 drops of vanilla or	
Caramel made of 3 tablespoonfuls of granulated sugar	20(?)
	<hr/> 500

Beat the egg slightly, add the sugar, salt, and hot milk slowly. Cook in a double boiler, stirring constantly, until it thickens a little (if cooked too long, the custard will curdle, but may become smooth again if set in a dish of cold water and beaten at once). Flavor and cool.

To make caramel: Put the sugar in a pan directly over heat and burn until a very dark brown. Dissolve in hot water or milk.

Baked custard:	Calories.
$1\frac{1}{2}$ ounces of milk sugar	160
6 ounces of milk	120
1 egg	80
Nutmeg or vanilla.	
Speck of salt.	
	<hr/> 360

Beat the egg slightly. Warm the sugar and milk, stirring constantly, add to the egg, strain into a custard cup, and flavor. Bake in a pan of water in a moderate oven until a knife when cut into it will come out clean (30 minutes to 1 hour).

³⁰ By previously dissolving the milk sugar in water, 72 grams of it may be put into a cup of coffee.

Bread pudding:	Calories.
1½ ounces of milk sugar	180
6 ounces of milk	120
1 egg	80
1 slice of bread ($\frac{3}{8}$ inch thick)	60
½ ounce of butter	120
	<hr/>
	560

Spread the bread with butter and cut into squares. Beat the egg slightly; heat the milk and sugar, stirring constantly; mix with the egg and pour over the bread. Grate nutmeg over the top, and bake the same as the custard.

Vanilla ice cream:	Calories.
4 ounces of cream	240
2 ounces of milk	40
2 ounces of milk sugar	240
Speck of salt.	
Few drops of vanilla.	
	<hr/>
	520

Mix the cream, milk, and sugar, and heat, stirring constantly, until the sugar is dissolved. Then flavor, cool, and freeze.

Lemonade:	Calories.
4 ounces of milk sugar ³¹	480
7 ounces of cold water.	
2 tablespoonfuls of lemon juice (or to taste).	

Boil the sugar and water for two minutes, add lemon juice to taste, strain, and cool.

ANALYSIS OF CASES. Conclusions drawn from statistical studies of typhoid fever are apt to be misleading unless the number of cases is large and unless they cover many years. Epidemics differ in severity, and the frequency of complications and relapses varies in different years. Yet the effect of raising the nutritive value of the diet in even a limited number of cases may furnish important evidence of the results to be anticipated in other cases. The fact that metabolism apparently follows normal laws in typhoid fever justifies a comparison of the effects of starvation in this disease with the effects of starvation in health. It is not necessary to starve the race in order to determine that starvation is detrimental. Analogously, if a few typhoid fever patients are benefited by improving their nutrition, the assumption that the majority will be, at least appears probable.

There are 111 cases in the series.

Character of Illness. Thirty-seven of the cases were mild, 43 were severe, and 31 were very severe.

Mortality. Eleven of the 111 cases died, giving a mortality of 10 per cent. The simple statement of the mortality, however, does not convey sufficient information regarding the cases. The mortality rate should be compared with that of cases on other diets in the same epidemics, and the characters of the disease in the cases furnishing the mortality should be considered.

³¹ Some patients have said the lemonade as prepared was not sweet enough, at which times 1 or 2 tablespoonfuls of cane sugar have been added.

For purposes of comparison, a table of all cases treated in Bellevue and Allied Hospitals during the period covered by this report is given (there were so few cases on the high calory diet in 1907 that they are not included in the computation).

Year.	B. H. and A. H. Total cases.	Total deaths.	Diet cases. Total.	Deaths.
1907	9	0
			—	—
1908	315	55	28	1
1909	258	37	39	3
1910	302	45	35	7
	—	—	—	—
	875	137	102	11 = 10.7 per cent.
	102	11		
	—	—		
	773	126 = 16.5 per cent.		

As will be seen from the table, 16.5 per cent. of all cases in Bellevue and Allied Hospitals in 1908, 1909, and 1910, exclusive of the cases on high calory diet, died, while 10 per cent. of the cases on this diet died.

It seems fair to assume that the type of infection in the different hospitals of the department was essentially the same in the same seasons.

In order that the character of the disease in the cases which died, and their relation to the diet may be appreciated, it will be necessary to give a brief clinical history of each case.

CASE I.—Series No. 11, 1908. E. S. Admitted on the tenth day of the disease; died on the thirteenth day; "walking typhoid;" heart in bad condition on admission; patient pale and dyspneic. Diet started on the eleventh day. On the twelfth day intense air hunger developed; the patient's face was drawn and cyanosed; heart sounds were faint, action irregular.

CASE II.—Series No. 47, 1909. W. S. Admitted on the seventh day of the disease with lobar pneumonia as a complication; died on the twentieth day. Has used alcohol to excess; became irrational shortly after admission. Temperature ranged up to 106° F. Diet was taken indifferently. Prognosis very grave from day of admission.

CASE III.—Series No. 51, 1909. C. McG. The patient had been on a ten-day spree, lasting until the ninth day of the disease; severe diarrhea during the debauch. Admitted on the fourteenth day with alcoholic gastritis and persistent nausea and vomiting. Food was taken indifferently. Perforation occurred on the twentieth day; operation was performed immediately; death on the twenty-fourth day.

CASE IV.—Series No. 74, 1909. A. S. Admitted on the eighth day of the disease; died on the fiftieth day. Temperature range high; dropped to normal on the morning of the thirty-fourth day, but evening temperature was never below 101° F.; rose in a few

days to its former high level. Persistent delirium and diarrhea. Developed double otitis media on the twenty-second day. Took food only fairly well.

CASE V.—Series No. 77, 1910. J. R. Admitted on the eighteenth day of the disease. Temperature very high; patient delirious. Developed pulmonary edema, and died on the twenty-second day. At autopsy, acute bronchitis, extensive bronchopneumonia, chronic otitis media, and acute parenchymatous nephritis were found as complications.

CASE VI.—Series No. 89, 1910. T. K. Very alcoholic on admission; irrational at times. History indefinite, probably in the fourth week of the disease. Persistent nausea and vomiting; unable to take much food. Passed a few small blood clots on the seventh day in hospital; severe hemorrhages on the ninth and tenth days. Complained of pain on right side of abdomen on tenth day; distinct mass palpable below umbilicus. Operation for supposed perforation showed this to be a malformed kidney lying across the brim of the pelvis. The patient had status lymphaticus. At autopsy, acute bronchitis and bronchopneumonia were found as complications.

CASE VII.—Series No. 91, 1910. J. S. Admitted on the fifteenth day of the disease. Has status lymphaticus. Patient resisted all treatment, and took very little food. Developed bronchopneumonia about the thirty-seventh day, and died on the thirty-ninth.

CASE VIII.—Series No. 92, 1910. T. R. Admitted on the ninth day of the disease; during the day the patient had an intestinal hemorrhage, and pulse became weak. On the following day the patient passed 20 ounces of dark-red blood. Developed diphtheria on the thirteenth day. Died on the twentieth day.

CASE IX.—Series No. 93, 1910. J. E. Admitted to surgical ward with abscess of prostate twelve days before the typhoid developed. Temperature fell slowly to normal after operation, but immediately rose again. Transferred to medical ward on the ninth day of the typhoid. Operation wound discharging up to the eighteenth day. Took diet well. Developed lobar pneumonia on the twenty-third day; died on the twenty-sixth.

CASE X.—Series No. 94, 1910. A. H. Admitted on the tenth day of the disease. Diet started at once and was taken well. Had severe intestinal hemorrhage on the fourteenth day; blood continued to appear until the twenty-first. On the twenty-second day the temperature dropped to 98° F.; respirations became rapid and shallow; patient died on the twenty-third day. The diet was stopped on the occurrence of the hemorrhages.

CASE XI.—Series No. 107, 1910. J. N. Admitted on the eighth day of the disease. Diet started at once; patient was hungry and took food well. The disease ran an unusually long course. Lobar pneumonia developed, and the patient died on the forty-fifth day.

These histories show that Cases IV, X, and XI were the only ones in which the diet had a fair trial. The other cases have not been excluded from the series because similar ones undoubtedly exist among those not on the diet (the details of which have not been accessible), and because of possible bias. If one excludes all deaths except Cases IV, X, and XI, the mortality rate is only 2.7 per cent.

The number of cases in the series and the length of time that the high calory diet has been on trial—four years—apparently justify the assumption that the mortality from typhoid fever may be reduced by maintaining the patient's nutrition at the highest possible level.

Relapses. Relapses occurred in 23 of the 111 cases, or in 20 per cent. The incidence of relapses by years was as follows:

	Cases.	Relapses.	Per cent.
1907	9	2	22
1908	28	10	39
1909	39	9	23
1910	35	2	5
		Average	20

The percentage of relapses in the first three years is so high that information was sought regarding their occurrence on the First Medical Division.³² The result is as follows:

	Cases.	Relapses.	Per cent.
1907	51	13	25
1908	31	10	32
1909	36	6	16
1910	46	15	32
		Average	26

I do not believe that one is justified in drawing any conclusion from the comparison of these statistics except that the percentage of relapses was high on both the milk and high calory diets among the cases cited. The comparison may indicate, however, that neither the milk nor the high calory diet has any effect upon the incidence of relapses.

Complications. Hemorrhage. The occurrence of hemorrhage in the different years was as follows:

	Cases.		Per cent.
1907	9	1 with hemorrhage	11
1908	28	5 with hemorrhage	17
1909	39	2 with hemorrhage	5
1910	35	4 with hemorrhage	11
		Average	12

³² I wish to express my thanks to the visiting physicians on this Division for the privilege of using these statistics.

Three cases complicated by hemorrhage died from other causes; 1 case died as the result of hemorrhages.

A striking fact has been observed in the cases complicated by hemorrhage. When the patient has been well nourished, the loss of blood has produced little, if any, more effect than the loss of a corresponding amount of blood would produce in a healthy man.

Other complications. Perforation occurred in 1 case, lobar pneumonia in 6 cases, otitis media (probably the lighting up of an old process in all instances) in 9 cases, bronchopneumonia in 4 cases, cholecystitis in 2 cases, pulmonary tuberculosis in 1 case, tuberculous abscess about rectum in 1 case, pleurisy in 2 cases, diphtheria in 2 cases, phlebitis in 3 cases, periosteitis in 1 case, panophthalmitis in 1 case, and abscess about rectum (non-tuberculous), 1 case.

Weights of Patients. Weights of the patients were taken usually every second or every third day, on a platform constructed for the purpose. The majority of the patients lost some weight during the course of the disease. The losses corresponded in general with the amount of food they were able to take. In the majority of cases the losses were under 10 pounds, and often did not reach 5 pounds. The greatest loss recorded was 20 pounds, between the ninth and twenty-second days of a thirty-one-day case. The attack was mild, though long, and the patient took his food well, reaching 3100 calories on the second day after admission, and 4000 later on. Some patients who lost flesh during the early stages of the disease, recovered it in the steep-curve period. Other patients gained 1 to 2 pounds during the febrile period, and several patients gained in weight during relapses. In some the weight remained stationary.

Gains in weight during the first two weeks of convalescence—when under the method of partial starvation patients usually continue to lose—varied from 3 to 10 pounds. In a few instances temporary losses of 1 to 3 pounds occurred in this period. A number of patients gained 1 pound a day; one gained 3 pounds in two days; one gained $5\frac{1}{2}$ pounds in three days; and one gained 9 pounds in five days.

As the gains in weight were retained by the patients even after the food was changed to the "regular" hospital diet, they may be assumed not to have been due simply to water retention.

The Individual Patient. The claim has been made from time to time that particular diets shorten the course of typhoid fever, but the evidence for such claims will not bear close analysis. No one can predict how long the fever will last in any given case. There is no reason to think that the high calory diet has had any influence upon the duration of the febrile stage of typhoid fever, but there is strong evidence that it modifies the course of the disease favorably. Though perhaps the majority of patients on the diet lose some flesh, the marked emaciation formerly so characteristic of the disease does not occur. Patients often retain their

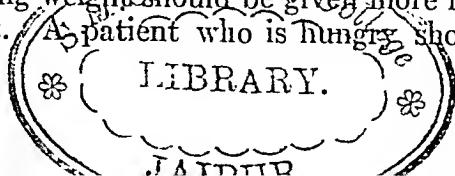
facial coloring throughout the disease. Mentally they are alert and take an active interest in their environment. Many of them have been permitted to read the daily papers and magazines without injurious effects. The so-called typhoid state has not developed in any patient who was able to take sufficient food, and has disappeared under the influence of the diet when patients have entered the hospital in that condition. I doubt if a physician glancing casually through the wards would be able to pick out the typhoid fever patients.

The patients have been stronger when they were permitted to get out of bed, usually two weeks after the fever subsides, than similar cases were formerly on the exclusive milk diet. They have left the hospital in shorter time and in better condition. While it has been difficult to follow the patients after they left the hospital, the limited information I have been able to obtain leads me to believe that convalescence has been materially shortened.

While I have believed for several years that the principles underlying the employment of the high calory diet in typhoid fever would be found applicable to other acute infective diseases, the value of the diet in such cases has not yet been tested sufficiently, so far as I am aware, to justify more than tentative recommendations. I have given the diet to patients with lobar pneumonia, but the number of cases has been small. Tympanites is so common in severe cases of pneumonia, and the respiratory distress it causes is so serious, that one should take especial care not to increase it through the careless administration of food. In all cases where it can be done safely during the course of the disease, and generally in convalescence from it, I would suggest that the energy value of the diet be increased by the addition of carbohydrates, though not necessarily milk sugar. The high calory diet has been found to be beneficial in the severer respiratory infections which are commonly called influenzal, and from which convalescence is often so slow. It has been employed with satisfaction in some chronic diseases accompanied by impaired nutrition, and there is reason to believe that it would be useful in severe septic infections and in some forms of pulmonary tuberculosis. But, as has been stated, the diet has not yet been thoroughly tested in any disease except typhoid fever.

CONCLUSIONS. 1. None of the older diets for typhoid fever furnishes the patient with sufficient energy for his metabolic exchanges. Therefore a patient taking any of these diets is compelled to live in part upon his own tissues.

2. The amount of food which a patient requires can be determined only by his individual needs. The clinical guides to these needs are the weight of the patient and the state of his appetite. A patient who is losing weight should be given more food if he can digest and absorb it. A patient who is hungry should be given



sufficient food to appease his appetite. In the early stage of severe cases it is always difficult to give more than 3000 calories a day; in the steep-curve period and in convalescence, patients take readily from 4000 to 6000 calories a day.

3. If any article of food causes persistent disturbances of digestion, the quantity given should be diminished, or the food should be stopped; otherwise the object of the high calory diet, the maintenance of the patient's nutrition, is defeated. If a patient cannot take all the food he requires, he should be given all he can digest and absorb.

4. Carbohydrates should furnish the greater part of the energy of the diet. The daily protein ration should not be below 62 grams, nor greatly exceed 94 grams. Clinical evidence indicates that a diet rich in fat may be taken by typhoid fever patients with benefit. Fat has furnished in some cases from one-third to one-half of the total energy of the food.

5. In the cases studied, the high calory diet has apparently modified the course of the disease, shortened convalescence, and reduced the mortality.

Finally, I wish to express my indebtedness and my thanks to Dr. Dana for the privilege of studying cases in his service, to Drs. W. Murray Kerr, T. J. Kearns, W. E. Lowthian, T. R. Pooley, Jr., Harold De Wolf, and William Tomkins, House Physicians in different years, for valued assistance, and to Miss Mary E. Sheehan, Head Nurse in Ward A1, for many practical suggestions and for her untiring aid in carrying out the administration of the diet.

MULTIPLE CONGENITAL HEMANGIO-ENDOTHELIOMAS OF THE LIVER.

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(From the McMane's Laboratory of Pathology, University of Pennsylvania.)

THE findings at autopsy in this case from the medical service of Dr. Le Boutilier, at St. Christopher's Hospital, Philadelphia, are so uncommon that we feel justified in placing the case on record. The subject was a female infant, aged ten weeks, one of twins, breast-fed. From birth a distention of the abdomen was noted which constantly and rapidly increased; the infant at the same time

became each day weaker. On examination, the liver was found greatly enlarged, extending to the umbilicus and possessing a palpably nodular surface. Otherwise physical examination proved negative. The urine examination and the Wassermann reaction were negative. The temperature was slightly subnormal. In the hospital the child continued to become weaker, and without further symptoms died.

Autopsy was performed on November 3, 1910, a few hours after death, by Drs. Veeder and Austin. The abstract of the protocol from the records of the McMane's Laboratory of Pathology is as follows:

Body of a fairly well-nourished female infant. Slight postmortem rigidity and cadaveric lividity present. Abdomen markedly distended.

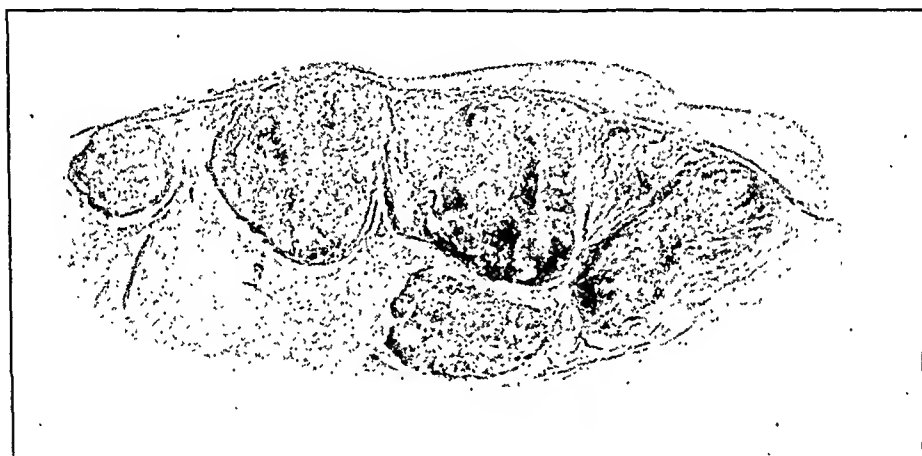
Abdomen. Primary incision showed a thin panniculus adiposus, no bleeding. Peritoneum smooth and glistening. Very slight excess of thin, clear fluid present in the abdominal cavity. No adhesions.

Liver. The liver was greatly enlarged, extending down as far as, and to the left of, the umbilicus, weighed 595 grams, and measured 17 x 9.5 x 6 cm. Its surface showed numerous dark, purplish nodules standing out prominently from the smooth peritoneal covering. These nodules varied in size from that of a pea to that of a horse-chestnut, were slightly umbilicated, and gave the liver an irregular, knotty appearance. Over the dome of the liver 19 of these nodules were counted, and on the under surface, 23. A typical nodule (2 cm. in diameter) had a dark red centre 1.4 cm. in diameter, surrounded by a white translucent zone 1 mm. in width. Outside of this was another dark zone from 1 to 3 mm. in width, apparently due to congestion, with radiations extending from it into the surrounding liver tissue. The nodules were distinctly softer than the surrounding liver substance, and were of about the consistency of brain. On section nodules were found throughout the substance of the liver. They showed, on cut surface, very dark, bluish-red centres, surrounded by a zone of pale white tissue from which branching processes extended inward toward the centre of the nodule. The liver tissue between the nodules was firm, quite yellow, somewhat congested, and showed the lobules faintly demarcated.

Sections of the tumor nodules and liver tissue were embedded and cut in paraffin, and stained with hematoxylin and eosin for microscopic examination.

Microscopic Description. The centres of the tumor nodules are composed of dilated blood spaces, irregularly arranged between numerous narrow trabeculae of fibrous tissue and atrophic liver cells. The endothelial cells covering the trabeculae are much more numerous than in the wall of a normal vessel, and in places have proliferated to form a double layer. They have large oval and

somewhat vesicular nuclei, and occasionally show mitotic figures. The blood spaces are densely packed with erythrocytes and a few leukocytes. Around each nodule is an irregular capsule of compressed and fibrosed liver tissue with atrophic and vacuolated liver cells. The capsule of Glisson persists, and shows considerable overgrowth of fibrous tissue, particularly about the bile ducts. At some points the dilated blood channels are apparently dissecting their way into the liver substance, and here a transition can be seen from the normal to the atrophic liver cells. In some places the tumor tissue comes into apposition with the capsule of the liver, while in others a moderate layer of degenerated liver cells and fibrous tissue intervenes. The liver tissue uninvolved by the tumor shows advanced fatty change, the cells being occupied by large vacuoles. The protoplasm stains poorly and is granular. The connective tissue of the parts of the liver uninvolved by the tumor does not show hyperplasia.



Cut surface of liver.

The heart, lungs, thymus, spleen, kidneys, pancreas, adrenals, and abdominal lymph nodes were examined both grossly and microscopically, and no lesions of any moment were found. The only other pathological findings, and apparently they bear no relation to the tumors, were two small ulcerations of the duodenum situated just beyond the pylorus, about 4 mm. in diameter, extending through the mucosa.

From the histological picture the diagnosis of cavernous hemangiomas is evident. The dark centres of the nodules, seen grossly, correspond to the large collections of blood between the newly formed and growing bloodvessel walls. The white encapsulating area corresponds to the surrounding band of fibrous tissue with its atrophic liver cells. The septa passing toward the centre of the nodules from the periphery are bands of overgrown fibrous tissue along the bile ducts and larger bloodvessels.

Angiomas of the liver are not uncommon, but have rarely been reported in infancy or childhood. Primary sarcoma and carcinoma are far more common in childhood, as is shown by the large number of cases which Steffan¹ was able to collect. In searching the literature we have frequently found the statement that angiomas occur often in childhood, but it is seldom that references are given or cases cited, and we are, therefore, inclined to attribute this statement to the assumption by the authors of a congenital origin for the angiomas found in adults rather than to the discovery of the tumor during early life.

Cases of solitary angioma in infants have been reported by Steffan,² Michailow,³ Kaufman,⁴ and others, in all, however, less than a dozen.

The number of cases reported of multiple hemangiomas of the liver in children is even smaller. We have, in fact, been able to find but 3. One of these, reported by Chervinsky,⁵ in an infant aged six months, is in many respects identical with ours. It was briefly as follows:

A child, born at term, of healthy parents, began to show enlargement of the abdomen a few weeks after birth. This increased, and before death, which occurred at the age of six months, a hard nodular tumor mass was palpable in the upper abdomen. Death occurred apparently from general weakness. There was no family history of syphilis. The autopsy showed the greater part of the abdomen to be occupied by the liver, which weighed 943 grams, and measured 22 x 10 x 6 cm. The liver showed nodules throughout varying in size from that of a pea to that of a hen's egg, deep red in color, and slightly umbilicated. On section the nodules were composed of a dark-red centre surrounded by a white ring, and some showed white fibrous bands running in from the periphery. Microscopically the centres of the nodules were composed of cavities, or spaces, lined by endothelial cells and containing red and white blood cells. The capsule was composed of fibrous tissue and atrophic liver cells, and was somewhat infiltrated with lymphocytes. The parts of the liver distant from the tumor showed some disintegration and an increase of perilobular connective tissue.

A second case, of similar type, occurring in a child, aged seven years (first noticed at the age of five and one-half years), was reported by Sawyer.⁶ In this case the family history was negative. The swelling of the abdomen was first noticed about a year and a half before death, and as it increased in size the child became emaciated and developed a slight fever. Autopsy showed no signs of congenital syphilis. Tuberculosis of the spleen, pancreas, and

¹ Geschwülste in Kindersalte, 1905.

² Ibid.

³ Archiv f. Kinderheilk., 1901, xxi, 291.

⁴ Spezielle Path. Anat., 1907, p. 579

⁵ Archiv. de Phys. norm et Path., 1885, vi, 553.

⁶ Rep. Soc. Study Dis. Child, London, 1906, vi, 19.

abdominal lymph nodes was present. The liver weighed about 900 grams, was nodular, and purplish in color. Microscopically, there was, throughout the liver, a widespread, nodular, angiomatous process. Between the nodules there was marked cirrhosis, with broad bands of fibrous tissue intersecting the liver and with prolongations surrounding the lobules. The diagnosis of angiomatosis with secondary cirrhosis was made.

The third case is described by Bruchanow.⁷ It was a case of multiple angiomatosis of the liver in an infant, aged fifteen weeks, who showed also a number of angiomatosis of the skin. At autopsy an enlarged liver weighing 710 grams, and measuring 20 x 14 x 6 cm., was found, which contained a number of nodular tumors varying in size from that of a pea to that of a hen's egg. According to Bruchanow, these were true growing, cavernous angiomatosis. His diagnosis was subsequently attacked by Schmieden,⁸ on grounds, however, which do not seem to us to be tenable. These 3 cases are the only ones resembling ours which we have been able to find in the literature.

Several theories have been offered to explain angiomatosis of the liver. For the majority of cases the old view that the tumor is the result of a capillary dilatation rather than a true blastoma is probably correct. Schmieden⁹ and Adami¹⁰ take this stand. Ribbert¹¹ and Bruchanow¹² explain the capillary dilatation as the result of a developmental defect, the bloodvessels having failed to establish normal relations with the liver cells. Pillet¹³ advocates a theory of fetal inclusion. Probably no one explanation will suffice for all cases. Our own case, as well as the 3 similar ones quoted from the literature, is probably more closely related to the tumors for which Mallory¹⁴ has recently advocated the name "hemangio-endothelioma." These he defines as angiomatosis which show distinct proliferation of the endothelial cells, the essential cell of the bloodvessel, with distinct new formation of bloodvessels, a true blastoma, therefore. The term was applied by Mallory¹⁵ particularly to those angiomatosis of the skin, which are not so uncommon, in which there is a true new formation of bloodvessels and which, as a rule, if recurrence is to be prevented, must be removed completely with a considerable portion of the surrounding tissue.

In our case the marked atrophy of the liver cells, the rapid increase in size of the liver, the young character of the fibrous tissue in the nodules, and, above all, the distinct evidence of endothelial cell proliferation, together with the clinical course of the case, all lead us to class the tumors as true blastomas, multiple congenital

⁷ Zeitsch. f. Heilk., 1899, xx, 131.

⁸ Loc. cit.

⁹ Virchow's Archiv, 1898, cii, 351.

¹⁰ Le prog. méd., 1891, No. 29, p. 50.

¹¹ Jour. Amer. Med. Assoc., vol. iv, p. 1621.

¹² Virchow's Archiv. 1900, clxi, 373.

¹³ Principles of Pathology, 1908, i, 751.

¹⁴ Loc. cit.

¹⁵ Jour. Exper. Med., 1908, x, 575.

hemangio-endotheliomas. Specimens of the tissue were submitted to Professor Mallory, of Boston, and to Professors Pearce and Allen J. Smith, of Philadelphia, who have confirmed the diagnosis and to whom we wish to express our thanks.

OBSERVATIONS UPON THE PERSISTENCE OF GONOCOCCI IN THE MALE URETHRA.

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SURELY none of us has any precise idea as to how long the gonococcus may survive in the glands that empty into the male urethra; for if they may survive a year or two, who shall deny them a decade? Not I, for one.

And yet I have not seen it. I have never known the gonococcus to survive in a male host for more than three years. I believe I could count upon my ten fingers the instances of a survival of eighteen months or more that have come under my observation. I recollect but one instance in which a year's treatment at my hands failed to free the urethra of gonococci. But I hasten to attribute this result to nature rather than to art. One of the most obstinate cases I ever undertook I treated for six months or more; he still had gonococci. He then deserted all treatment for six months. Then he married, and soon thereafter returned to show me that he was, so far as I could tell, entirely well. To be brief, I believe that the gonococcus does not persist in the male urethra for more than three years, while in at least 90 per cent. of cases it disappears, with or without treatment, within a year.

Upon what is this opinion founded? Not upon the cases and statistics to be cited. These do but illustrate and in some measure confirm my opinion. But this opinion is founded upon a double basis. First, my own inability, in spite of an alert interest in the subject for more than a decade, to find exceptions to the rule; and secondly, the insufficient evidence upon which exceptions are alleged either by physicians who have seen individual patients before they reached my hands, or by those who write.

What, then, is sufficient evidence that the male urethra is or is not free from gonococci?

We may divide the patients who come with this question upon their lips into four classes, as follows:

1. Patients who have apparently been cured at least three months of a gonorrhea and who show (a) no purulent shreds or free pus in the morning urine, and (b) no pus in the secretion expressed from prostate and vesicles. The observation of the

clinician is sufficient to declare such patients clean without any laboratory confirmation.

2. Patients (usually acute cases) in the same condition, but whose probation of three months has not elapsed. To declare these well the clinician must be fortified by an expert examination for the gonococcus, which should not be made until the patient has remained entirely well without treatment for at least two weeks.

3. Patients (usually with a chronic pearly morning drop) with mild chronic anterior urethritis and perhaps superficial posterior urethritis as well, and who show (a) purulent shreds, but (b) practically no free pus in the expressed prostatic vesicular secretion. Such patients are usually gonococcus-free, but their clinical diagnosis requires expert laboratory confirmation.

4. Patients with free pus in the urine, which in chronic cases is usually in large part from the prostate or vesicles.

The presence of gonococci in such cases is suggested by the occurrence of complications (acute urethritis, prostatitis, epididymitis, rheumatism, etc.) either spontaneously or as a reaction to local (sounds, injections, sexual intercourse) or general (alcohol, exercise) irritation. Yet such clinical signs have no absolute value in diagnosis, for among the most irritable types of urethritis are certain non-gonococcic ones, while certain urethræ, though still harboring gonococci, are benefited by exercise, alcohol, sexual intercourse, and sounds.

This class of cases, therefore, always requires laboratory diagnosis.

TECHNIQUE OF CLINICAL EXAMINATION.

For the clinical examination the patient partially empties his bladder, submits to a thorough prostatic massage, delivers a drop of the expressed secretion upon a slide, then empties his bladder. The clinician then examines for pus (1) the discharge (if there be any), (2) shreds fished from first urine, (3) centrifuged first urine, (4) expressed prostatovesicular secretion, (5) centrifuged second urine. A few white cells per field do not justify the diagnosis "pus."

I commonly employ the sound, alcohol, and physical exercise in the treatment of chronic urethritis, but not directly for a gonococcus diagnosis. Yet most of my patients have been tried by these irritants in the course of treatment before coming to the final test.

The chief care of the clinician should be not to attempt too accurate a diagnosis. Pus he can readily identify, and from the presence or absence of pus derive inferences accurate up to a certain point. It is in overstepping this limit, in attempting a direct gonococcus diagnosis by the limited means at his command, that he errs.

There is an oft-quoted statement to the effect that the gonococcus may be accurately diagnosticated by the Gram stain¹ in 95 per cent. of cases. What is this "5 per cent." of error? Most of us have attributed it, I fancy, to errors in technique, in preparation and staining of the specimen, etc. But all such sources of error may be eliminated without making the Gram a perfect differentiating stain. There remain an astonishingly large proportion of cases of non-gonorrheal urethritis, the examination of whose pus in smears by a truly expert bacteriologist discloses the presence of bacteria more or less closely resembling the gonococcus. Thus, among the 102 examinations by smear and culture recorded in the tables herewith, made for me by Prof. Elser and Dr. Huntoon, of the Cornell Medical School, 18 showed gonococci (6 of them by smear alone), while 15 showed bacterial forms more or less closely resembling the gonococcus when stained by the Gram method, and required further evidence to identify them precisely.

Pray do not overlook the fact that in one and the same sentence I question the precision of diagnosis by smear alone for 15 cases, and yet grant it accurate for 6 others. For in certain cases the gonococci are so numerous and typical in the smear that even though one fails to cultivate them (for reasons to be discussed later), the diagnosis from such smears may be accepted as entirely adequate.

But, to get back to our original proposition, the clinician does not check up his observations by careful cultures, and to his eye every Gram negative intracellular coccus is a gonococcus. Indeed, many doubtless omit the formality of a Gram stain. Under such circumstances a positive diagnosis of gonococci is justified only in the presence of *both* of two conditions, namely, (1) clinical evidence of gonorrhea, and (2) the presence of numerous, typical gonococci.

These conditions are always fulfilled in cases of uncontrolled acute urethritis, and for the diagnosis of these the clinician need scarcely ever enlist the services of the bacteriologist. But chronic or nearly cured urethritis often fails to present sufficiently clean-cut features to justify a positive or negative diagnosis from the clinician. Indeed, so little faith do I put in my own bacterial

¹ The Gram stain is so frequently carried out in a loose and inaccurate manner that it seems worth while to note the method of staining employed at the Cornell laboratories. It is essential for the success of this stain that the various steps be measured by the watch. The film, after fixation by heat, is treated with an aniline-water, gentian-violet solution for a period of three minutes, blotted and a Lugol solution applied for two minutes. The film is again blotted and washed in absolute alcohol for thirty seconds. In the case of spreads made from exudates, differentiation in absolute alcohol is continued for a longer period, the time allowed depending upon the thickness of the film. As a counter-stain, a very weak watery solution of basic fuchsin is employed, which is allowed to act for thirty seconds. The aniline-water, gentian-violet solution is made up according to the following formula: Aniline water, three parts; absolute alcohol, seven parts; distilled water, ninety parts. This mixture is thoroughly shaken and filtered through a well-moistened filter. To the clear filtrate add 2 grams of Grubler's powdered gentian violet, shake well, and set aside for twenty-four hours. For staining purposes, pipette off the supernatant fluid, which obviates the necessity of filtration. This solution will keep for from four to six weeks, and does not immediately deteriorate, as is popularly supposed. A watery solution of Bismarck brown gives a better counter-stain than the basic fuchsin, unless this is employed in very weak solution to avoid over-stain. Unfortunately, the brown has to be made up fresh.

diagnosis of chronic urethritis that I do not waste time to make more than one examination of a doubtful case. If that is negative, or if the urethritis is apparently cured or non-gonorrheal, I intrust the bacteriological diagnosis to the laboratory.

Such being my point of view, I need pretend no sympathy with the conclusions of those writers who, flying in the face of clinical facts, found a diagnosis of gonorrhea, years after a clinical cure, upon a few Gram-negative intracellular cocci. Indeed, patients upon whom this type of unjustified diagnosis has been made and physicians who put faith in these reports are, as you well know, among the woes of the specialist.

BACTERIOLOGICAL EXAMINATION.

So much for the clinician. The bacteriologist's diagnosis stands upon a totally different basis. By smear and culture he can usually distinguish the bacteria present in the fluids submitted to him. Thus he may err, through his own fault or through the fault of the clinician who submits the specimens to him, and the precision of his diagnosis depends upon a well-prepared specimen as much as upon his own skill. This double point of view is peculiarly important to our understanding of gonococcus diagnosis. A "well prepared" specimen must be fresh, for there is grave probability that gonococci that have remained in cool urine for half an hour cannot be cultivated. Moreover, it must cover the ground, notably the prostate and vesicles.

The technique I at present employ (and have employed in cases 1 to 35 and 67 to 86 of the present series) is the following:

1. Sometimes the patient takes a smear of his morning discharge, but this is usually of little interest.

2. He retains his urine three or four hours, if possible, and then comes to the office, has his glans penis washed with boric acid solution and passes part of his urine (about 100 c.c.) into a large sterile test-tube. This he keeps warm by putting it in his vest pocket when he dons his clothes.

3. I then thoroughly massage the prostate, vesicles, and membranous urethra, and send the patient immediately to the laboratory, where he urinates the material expressed from the internal genital glands into a sterile test-tube. This is promptly centrifuged and examined. All smears are stained by the Gram method. Cultures are made upon ascitic agar streaked with aged human blood serum and upon other media.

By this method the contents of the important posterior urethral glands are not obtained absolutely uncontaminated, yet the admixture of rapidly growing urethral organisms is reduced, and the smears tell quite accurately the preponderance of bacteria in each specimen. In 6 instances gonococci were found in the second

urine passed and not in the first, and 8 times this second urine was sterile while the first urine passed was infected.

But the possibilities of error on the part of the bacteriologist are not exhausted with proper preparation of the specimen. Recognizing that all microscopes are much alike, we are prone to forget that the bacteriologist, the man behind the gun, has as much personality as the physician. Bitter experience has taught us that the very best opinion is the only one worth having.

Yet even the best bacteriological skill may err or may fail to reach a conclusion.

Smears may be inconclusive either because they show: (1) Typical gonococci, but so few in number as not to justify a diagnosis (Cases 46 and 61); (2) bacteria resembling gonococci (Cases 26, 45, 49, 60, 63, etc.); (3) so many bacteria that the bacteriologist fears the gonococci may be concealed by them. Difficulties 1 and 2 are solved by culture or by repeated examination; 3, by local treatment of the urethra to reduce its flora.

Apart from the common laboratory accidents, cultures may fail because they are so overrun with rapidly growing organisms. These may act either by inhibiting the growth of the gonococcus, or by making the isolation of the same impossible.

Whereas the gonococcus was identified 6 times in the smears only (Cases 18, 27, 50, 53, 54, and 59), it was twice (Cases 53 and 55) identified in culture only.

Among the Gram-negative cocci that have been encountered in connection with the human being, the only one that is of interest to us is the *Micrococcus catarrhalis*. This organism closely resembles the gonococcus in its morphological characteristics, and in its predilection for the interior of leukocytes.

Cultural examination alone, therefore, can differentiate this organism from the gonococcus. The peculiar biochemical properties of this organism have been studied by von Lingelsheim² and Elser and Huntoon.³

Happily, the *Micrococcus catarrhalis* is very rarely found in the urethra. I have seen it in only one case (not in this series).

Apart from the *Micrococcus catarrhalis* it must be emphasized that in a small percentage of cases the normal urethra (and in a somewhat larger percentage the normal vagina) contains Gram negative cocci which, as a rule, can be differentiated from the gonococcus by their form, size and extracellular position. These organisms fail to grow on the usual culture media.

In one case in the present series (Case 72), an organism known as the *Diplococcus crassus* was encountered. This micrococcus is Gram variable in its reaction, and for this reason its identification is somewhat difficult.

Finally, a rather fruitful source of error remains to be mentioned, namely, degeneration forms of Gram-positive cocci. In examining

² Klin. Jahrb., 1906, xv, Heft 2.

³ Jour. of Med. Research, 1909, xx, No. 4.

films from the urethra stained according to the Gram method, one not infrequently finds organisms which do not retain the dye. The question then arises whether we are dealing with Gram-negative cocci or with altered or degenerated forms of Gram-positive cocci. This question, of course, can only be answered by culture. Such degenerated cocci were found in eleven of my cases.

Thus, even the most competent bacteriological examination may leave the clinician in doubt, for a time at least, and require, if only to save time, laboratory information of another sort.

COMPLEMENT DEVIATION TEST.

Until within the last year we have possessed no such test, but now in the complement deviation test for gonococci devised by Dr. H. J. Schwartz, of Cornell, we have a most excellent means of diagnosis. Since Drs. Swinburne and Schmidt have contributed upon this subject, I need not delay to expound the technique, and shall confine myself to a brief review of my experience with it.

Within its limitations I have found the complement deviation test singularly accurate. But its limitations must be borne in mind. It records the reaction in the blood to an inflammation which is confessedly often very localized and superficial. Consequently we must not expect too much of it in early or mild cases of urethral gonorrhea. On the other hand, if this blood reaction becomes marked, and persists for many months, it may continue positive for an indefinite time after the gonococci have disappeared.

Hence certain rules may be laid down for the interpretation of Dr. Schwartz's test, as follows:

1. A positive reaction in the blood may not be looked for until the gonorrhea has persisted long enough to produce such a reaction. This usually requires about a month.

I have obtained a reaction in twelve days (Case 6), and in another instance a negative reaction after two weeks (Case 21, II).

A gonorrhea controlled from the outset, or chronic and mild, might be expected not to give a blood reaction. Yet such is rarely, if ever, the case. Case 9, a gonorrhea so well controlled by pro-targol for four weeks that I thought it cured, showed a strong positive blood reaction and gonococci in the prostatic secretion. On the other hand, no case of chronic gonococcic urethritis has failed to give a positive reaction, save one (Case 22), in which a mild gonorrhea of seventeen months' duration gave a + - reaction, followed six and one-half weeks later by a reaction so weak as to be, in Dr. Schwartz's own words, "practically negative." Yet eight weeks later, without confessed or apparent reinfection, the reaction was strongly positive and gonococci were found.

2. A chronic gonorrhea, especially if severe, may or may not leave a persistent reaction for a period of weeks or months, the limitations of which have not yet been determined.

Dr. Schwartz estimates six weeks as an average maximum allowance. Yet I have seen two striking and authentic instances of blood reaction persistent for months.

The first (Case 10) was a most virulent initial gonorrhea of eleven months' duration, during many months of which time the patient was practically confined to the house by subacute pyelonephritis. This patient was free of pus and apparently cured in May, 1910. Prof. Elser at that time could find no gonococci. Yet seven months later the complement deviation reaction was strongly positive, and two months thereafter negative, the patient having taken no treatment and manifested no evidence of disease throughout this time.

Case 25 consulted me for persistent relapsing urethritis. Prof. Elser was unable to find gonococci, and I, attributing his troubles to prostatitis, relieved him by a brief course of prostatic massage. Yet Dr. Schwartz obtained a positive reaction and repeated this two months later, though the patient had been without symptoms or treatment all this while. Six weeks later, however, the complement deviation reaction was negative.

Hence dependence upon the complement deviation reaction exposes one to the possibility of delaying the guarantee of cure for several months. Yet occasionally, as in the cases above cited, clinical and bacteriological evidence may combine to warrant the assurance of a cure before the blood becomes negative. Otherwise one must wait.

But if the complement deviation test is so accurate, may we not substitute it for the bacteriological examination? It were premature to answer this question in the light of our present experience.

The complement deviation test has been proved wrong in 1 examination (Case 8) out of 47; the bacterial test once (Case 15) in over 100 examinations. For brief gonorrheas successfully treated by the repressive (commonly called abortive) injections one must depend chiefly upon the bacteriologist; for all others it is safest to employ both.

But the complement deviation test opens up new possibilities for solving medicolegal problems. Let me cite an example:

Case 21 was a married man who had acquired a gonorrhea several months previously, and had infected his wife. No gonococci were found in the urine, and he was declared free from infection, although his urethritis was not cured. His wife was also examined and pronounced cured. No blood test was made upon either. Yet six months later he returned, denying extramarital exposure, but showing a fresh gonorrhea two weeks old. Both he and his wife immediately submitted to the complement deviation test, and both were negative. Four weeks later he was positive and she negative, while she remained clinically clean. This development of a positive reaction in him showed his infection to be a fresh one due to extramarital exposure, in spite of his fervent denials.

TABLE I.—Diagnosis by Blood Examination.

Case No.	Number of gonorrheal infections and duration of present attack.	Clinical condition and date of subsequent examinations.	Blood.	Bacteria.
1	? , 3 months.	P. G. U. ²	+	Strepto. and Gram neg. bac.
2	1, 2½ weeks	Well; 1 week. 2 weeks later. 4 weeks later.	— 0 0	No gonococci. No gonococci. No gonococci.
3	I, brief.	Cured; 4 yrs. Stricture.	—	No examination.
4	I, 18 months.	Well; 18 months.	—	Gram neg. cocco bacilli (colon?). Few strepto.
5	III, ?	Cured; 7 years. Simple urethritis.	—	No examination.
6	I, 12 days.	Cured. 4 weeks later. 12 weeks later.	+ — + — —	Proteus, staph. and streptococci.
7	?	Stricture; 7 years.	—	No examination.
8	I, brief.	Well a year. 8 weeks later. 12 weeks later.	+ — 0	Staph. aureus and albus. Strepto. and Staph. albus.
9	II, 4 weeks.	Cured; pus in prostate. 1 week later. 3½ weeks later. 4 weeks later. 1 week later. 4 months later.	+ + 0 0 0 0 0	I, Staph. albus; II, gonococcus. Same as above. II, staph., degenerated forms. Streptococci. II, streptococci.
10	I, 11 months.	Just well. 7 months later. 2 months later.	0 + + —	Staph. and pseudodiphth. bac.
11	I, brief.	Well; 3 years. Pus in prostate.	— 0	I, Staph. albus and pseudodiphth. bac. II, same and small Gram neg. bac., degeneration forms in films.
12	I, 6 weeks.	Cured.	—	No examination.
13	III, brief.	Cured; 3 months.	—	Staph. albus and strepto.
14	II, 1 year.	Probable P. G. U. 3½ weeks later. 4 weeks later.	+ 0 +	Staph. albus and strepto. Sterile.
15	II, 5 years.	P. G. U. 1 week later. 6 months later.	+ — 0 —	I, Staph. albus and pseudodiphth. bac. II, same and gonococci. Staph. albus; II, sterile. I, pseudodiphth. bac.; gonococci (?) ; Cultures failed.
16	? , 7 years.	9 weeks later. Gonorrhea.	— +	Sterile.
17	I, brief.	Cured; 18 years.	—	I, sterile; II, gonococci in smears.
18	I, 4 months.	Gonorrhea. 5 weeks later, cured. 2 weeks later.	0 — 0	pseudodiphth. bac. II, Staph. albus. II, pseudo-diphth. bac.
19	II, 1 month.	Cured; 18 months.	—	Staph. albus and strepto.
20	?	P. G. U.	—	I, streptococci; II, sterile.
21	I, several months.	P. G. U. 3½ months later. 4 weeks later.	0 — +	I, pseudodiphth. bac.; II, sterile. Gonococci.
22	II, 17 months.	P. G. U. (?) 6½ weeks later. 8 weeks later. Later.	+ — + — +	Gonococci and Staph. albus. No gonococci.
23	I, 10 months.	P. G. U.	—	Staph. albus and strepto.
24	II, 18 months.	P. G. U.	—	
25	Many relapses.	P. G. U. 11 days later. 7 weeks later. 6 weeks later. Gonorrhea.	+ + 0 + — 0	I, staph. and pseudodiphth. bac.; II, staph. cultures failed. II, sterile.
26	II, 3 months.	9 months later; P. G. U.	+ —	Staph. albus and pseudodiphth. bac., gonococci (?) Same and strepto. and xerosis bac., but probably no gonococci.
27	I, several months.	7 weeks later. P. G. U.	+ — + —	Strepto. and pseudodiphth. bac., gonococci in smears only.
28	? , 1 month.	Cured; 6 months.	—	
29	I, 1 year.	P. G. U.	—	
30	I, 15 months.	Cured; 2 months.	—	Bac. capsulatus mucosæ.
31	III, 1 week.	P. G. U.; 10 months.	—	Degeneration forms in plates. Cultures sterile.
32	I, 2 months.	Cured; 1 year.	—	
33	I, 6 months.	Cured; 3 years.	—	
34	? , 1 year.	P. G. U.	+	

² P. G. U. = postgonorrheal urethritis.

TABLE II.—Diagnosis by Bacterial Examination.

Case No.	Number of gonorrheal infections and duration of present attack.	Clinical condition and date of subsequent examinations.	Bacteria found.
35	II, 2 months.	Cured.	Staph. albus. and strepto.
36	?, 1 year.	P. G. U.	Staph. albus.
37	?, 6 weeks.	Cured. Pus in prostate.	Staph. aureus.
38	II, 3 months.	P. G. U.	Staph. albus and aureus and strepto.
39	I, 2 months.	Cured.	Staph. albus and aureus and strepto., proteus and pseudodiphth. bac.
40	?, 6 weeks.	Cured.	Bac. coli.
41	?, 7 weeks.	Cured.	Staph. albus and strepto.
42	II, 3 weeks.	Cured.	I, staph. albus and aureus; II, Staph. albus.
43	?, 7 weeks.	Cured.	Staph. albus and a small Gram neg. bac.
44	?, 3½ weeks.	Cured.	Strepto. mucosæ.
45	?, 2 months.	Cured.	Staph. albus and strepto., pseudodiphth. bac. and a small Gram neg. extracellular coccus, not morphologically resembling gonococcus.
46	II, 3 weeks.	Cured; stricture. 11 weeks later.	Strepto., staph. aureus, and pseudodiphth.; on smear one pair of gonococci (?). I, Staph. albus, strepto., and pseudodiphth. bac.; II, no strepto.; otherwise same.
47	?, 4 months.	Cured.	Staph. albus.
48	?, 2 weeks.	Cured; relapse a week later.	Staph. albus and strepto.
49	II, 7 weeks.	P. G. U. 2 weeks later.	Staph. albus and gonococci. Staph. albus and strepto. and pseudodiphth. bac.
50	?, 6 months.	P. G. U. 1 month later.	Bac. coli, staph. and gonococci (in smear). Bac. coli, staph.
51	?, 6 months.	Cured.	I, staph. albus, Gram pos. bac.; II, sterile.
52	II, brief.	Cured; 6 years.	Staph. albus, strepto.
53	I, 4 months.	Cured.	Staph. aureus, strepto., Gram pos. bac.
	II, brief.	Cured.	No examination.
	III, 2 months.	Cured.	I, Staph. aureus; II, same and gonococci (in smear).
		3 days later.	Same except that gonococci appear only in cultures.
		18 days later.	I, Staph. aureus and pseudodiphth. bac.; II, staph. aureus, degeneration forms.
54	?, 1 year.	P. G. U. 19 days later.	Staph. aureus, strepto., and gonococci.
55	?, 4 months.	P. G. U. 1 month later.	Same; but gonococci only on smears of I. I, Staph. albus; II, Staph. albus and gonococci by culture only.
			II, Staph. albus and strepto.; II, Staph. albus.
56	I, 3 years.	Urethrorrhea.	I, Staph. albus; II, sterile.
57	?, 5 years.	Cured.	Staph. albus, strepto. and pseudodiphth. bac.
58	?, brief.	Cured; 1 year.	I, Strepto., pseudodiphth. bac. and degeneration forms; II, strepto., staph. albus, and degeneration forms.
59	?, 3 months.	Cured; 3 months.	Staph. aureus, strepto., gonococci in smears.
60	I, brief.	Cured; 18 months.	Staph. albus, strepto.
61	I, brief.	Cured; 3 years.	Staph. albus, strepto., and pseudodiphth. bac. - In I, by smear, a single-cell containing gonococci. Also degeneration forms.
		7 weeks later.	I, Staph. albus, and pseudodiphth. bac.; II, Staph. albus.
		2 weeks later.	I, Staph. albus, strepto., pseudodiphth. bac.; II, Staph. albus, pseudodiphth. bac.
62	I, brief.	Cured; 6 years.	Staph. albus, strepto.
63	?, 5 years.	Relapsing P. G. U.	I, Staph. albus, strepto., and intracellular degeneration forms (?) in smear. II, Staph. albus.
64	?, 3 years.	11 days later. P. G. U.	Staph. albus.
65	I, brief.	Cured; 10 months. 1 week later.	I, Staph. albus; Staph. albus and pseudodiphth. bac.
		17 days later.	Staph. albus and strepto.
66	I, Several mos. Well 3 years.	P. G. U.	Staph. albus.
67	I, well 3 years.	Cured.	Staph. albus, strepto., pseudodiphth. bac. Staph. albus, strepto.
			Sterile.

TABLE II.—Diagnosis by Bacterial Examination—(Continued).

Case No.	Number of gonorrheal infections and duration of present attack.	Clinical condition and date of subsequent examinations.	Bacteria found.
68	II, 3 weeks.	Cured.	Bac. prodigiosus and Gram pos. cocci.
69	?, brief.	Cured; 2 years.	Gram. pos. cocci.
70	?		Staph. albus.
71	I, 6 months.	Cured; 1 month.	Staph.
72	II, 3 months.	Cured. 2 weeks later.	Staph. albus, diplococcus crassus. Same.
73	I, 6 months.	Cured; 1 year.	Streptococcus mucosæ.
74	I, brief.	Cured; 3 years.	I, Staph. albus; II, sterile.
75	III, 7 weeks.	Cured.	Staph. albus and Gram pos. bac.
76	?, 8 years.	P. G. U.	Bac. coli. com.
77	I, 2 years.	P. G. U.	Staph. albus and strepto.
78	No gonorrhea.	Simple urethritis.	Pneumococci.
79	I, 1 year.	Gonorrhea. 1 month later; cured.	Staph. albus, gonococci. Staph. albus and strepto.
80	I, few weeks.	Well 2 months	Staph. albus, degeneration forms.
81	I, few months.	P. G. U.	Staph. albus, strepto., gonococci, and unidentified bacilli.
		I month later.	Gram. pos. bac.
82	III, 6 weeks.	Cured.	Staph. albus, Gram neg. bac.
83	?		Staph. albus, strepto., degeneration forms.
84	?		Strepto, pseudodiphth. bac.
85	II, 3 months.	Cured; 4 months.	I, Staph. albus, pseudodiphth. bac.; II, sterile.
86	I, 3 months.	Cured.	Staph. albus, pseudodiphth. bac.

DURATION OF GONORRHEA.

The tables herewith classify briefly the results of laboratory investigation of 86 patients clinically cured, or nearly cured, of urethral gonorrhea (Cases 21 and 53 twice investigated). Thirty-six were investigated by the complement fixation test, 77 by smear and culture. In 5 instances the patients were believed to be still infectious, and this belief was borne out by the laboratory findings; in 26 the patients had active urethritis, believed to be postgonorrheal (P. G. U.), yet in 8 of them gonococci were found. But among 51 with clinical evidence of cure (only shreds or light haze in urine), only 2 (Cases 9 and 53, III) showed gonococci, both of them brief cases temporarily controlled by repressive injections, while 1 (Case 48) was passed as clean by both clinic and laboratory, yet relapsed, and gonococci were found a week later. The relapse did not appear to be a new infection. Hence I estimate about 4 per cent. of clinical error in cases apparently cured. However, in 10 cases (1, 15, 16, 22, 26, 27, 49, 53, 54, and 59) the clinical presumption of cure was not fully certified by the laboratory findings.

Nevertheless, with all allowance made, I feel justified in stating that in 64 cases gonococci disappeared in less than a year, in 7 others with urethritis, examined from two to eight years after the onset, gonococci were not found, while in 6 (4, 22, 26, 34, 54, and 79) gonococci persisted from one to two years.

In almost all cases these conclusions were verified by clinical

examination of the patient a month or so after the cure had been pronounced. Moreover, I had the opportunity of examining 9 cases cured of gonorrhea from two to eighteen years previously (Cases 3, 5, 11, 17, 33, 52, 62, 69, and 74). In none of them were gonococci found, though the misleading "degeneration" forms of staphylococci appeared in Case 11.

Only twice were gonococci found in cases of urethritis of more than two years' duration. Case 16 had for several years suffered more or less constantly from a urethral discharge, with exacerbations, and with promiscuous cohabitation galore. Gonococci were found and attributed to a recent infection.

Case 15, on the other hand, had a single urethritis five years ago in which frequent examinations by the late Dr. Otis failed to reveal gonococci. He denied having had sexual intercourse with his wife or any one else for the whole five years. He came to me, having consulted no one in the two years since Dr. Otis' death. My clinical examination revealed only a mild chronic urethritis, but Prof. Elser found gonococci, and the patient went home (100 miles from New York), infected his wife, and developed an acute gonorrhea himself. Curiously enough in this case, Prof. Elser made his one error, pronouncing the specimens gonococcus-free⁵ on a second examination. But happily before I communicated this report to the patient his new infection had blossomed, and six months later he was apparently back to his mild chronic catarrh, as was his wife, and Prof. Elser declared him probably gonococcus-free. Yet the blood was positive. But nine weeks after this it was negative. My diagnosis of this case is that the patient is an amiable liar.

All of us have encountered cases such as these; we must perforce interpret them as fairly as possible in the light of all other cases. I have never seen one of them that convinced me he had harbored gonococci more than three years.

⁵ The laboratory does not guarantee the patient, but only the specimens submitted. Yet with this one exception Prof. Elser has always found gonococci in specimens from patients harboring them.

REVIEWS

ELECTRICITY, MEDICAL AND SURGICAL. By CHARLES S. POTTS, M.D., Professor of Neurology, Medico-Chirurgical College, Philadelphia. Pp. 509; 356 engravings, and 6 colored plates. Philadelphia and New York: Lea & Febiger, 1911.

WHILE claims that are ridiculously absurd have been made by writers on electricity, it is obversely true that of recent years investigations in this department of medicine have revealed a much wider range of usefulness for the electrical current than is generally believed. Dr. Potts is admirably qualified to write on this matter, not alone because of his vast experience in such work, but also by reason of his common sense views on the subject.

In this volume the heretofore separate consideration of the physiological action, the therapeutic uses, and methods of application of each form of current is abandoned, and these subjects are discussed collectively; therapeutic measures are similarly described. In these and in other ways the plan of the work is original, and the author's belief in the value of such methods, which are scientific rather than empirical, is well borne out in the text. This departure, however, would be somewhat confusing if it were not for the generous use of cross references.

The whole subject is comprehensively considered in seven sections, comprising electrophysiology, electrodiagnosis and electroprognosis, general electrotherapeutics, methods of obtaining general and local effects by the indirect action of electricity, and special electrotherapeutics, together with opening and closing collaborate sections on physics and the x-rays respectively.

Under electrophysiology is given a very useful chapter in which is summarized the physiological action of the various electrical modalities. In the matter of the sinusoidal current, Kellog receives credit for its early use; this enthusiastic physician is not too abundantly quoted, but perhaps some of his observations on physical therapy need further confirmation.

The important subject of electrodiagnosis is one of the best portions of the volume, and in the actual study of the motor points the reader is aided by the insertion of the invaluable plates from Mosher's *Electrodiagnosis*.

Special electrotherapeutics is given the most space. Here are considered diseases of the nervous system, muscles and joints,

thoracic and abdominal organs, bloodvessels, eye, throat, nose and ear, skin, and the genito-urinary organs, both male and female. A feature of this portion of the work is the illustrating of much special apparatus for use in the application of the current.

Methods of obtaining general and local effects by the indirect action of electricity is a useful section, and vibration is mentioned among other subjects; but we should like to see this given systematic consideration, as is done with heat and light. The more general use of vibration has found expression in the various apparatuses of Zander, and even massage and exercises are given indirectly through the current; abroad numbers of institutions are devoted wholly to such work, and this matter seems worthy of some mention. It is true this part of the volume only deals indirectly with electricity, but the field of physical therapy is not yet given proper consideration in other medical works; therefore we believe the value of this volume would be enhanced by some amplification of this subject.

The electric hot air douche has a distinctive use; it is both palliative and curative, and its application is unattended by pain. We do not see this mentioned, but such an apparatus may be procured, and with it an attachment which delivers an alternate hot and cold blast; this is vastly superior to the older methods.

The final section is on the x -rays, and appears to be well written throughout; the specialist contributing this portion believes in self-preservation, and wisely.

The writer of this book does not loiter on the by-ways, but prefers rather to keep the practical use of the current constantly before the reader.

The illustrations are exceptionally well chosen for the elucidation of the text, and the volume meets the requirements of the student, physician, surgeon and specialist.

It is the best work in English on the subject of electricity with which we are familiar.

N. S. Y.

CONTRIBUTIONS TO MEDICAL SCIENCE. By HOWARD T. RICKETTS, 1871 to 1910. Published as a tribute to his memory by his colleagues, under the auspices of the Chicago Pathological Society; pp. 497; 23 illustrations. Chicago: The University of Chicago Press, 1911.

As indicated in the title, the book is essentially a collection of the publications of Dr. Ricketts and of other workers inspired and directed by him. The work of collecting and classifying the numerous papers was carried on by a committee composed of Drs. Ludvig Hektoen, Preston Kyes, E. R. Le Count, George H. Weaver, and

H. Gideon Wells. The various publications are arranged in well-defined groups which follow one another in the same sequence in which Dr. Ricketts, during his life as an investigator, took them up. With the exception of a few papers which were not included in the book because of limitation of space, the studies presented cover the work in cutaneous blastomycosis, immunology, Rocky Mountain spotted fever, and the tabardillo of Mexico. The whole is unified to a certain degree by the insertion, at the beginning of the book, of an address delivered at the University of Chicago, by Dr. Ludvig Hektoen, on the occasion of the memorial services to Dr. Ricketts.

As indicated above, Ricketts' earlier work was in the field of dermatology, and the first studies presented are those on blastomycosis, or as Ricketts, apparently with great propriety, named the condition, *oidiomycosis* of the skin. Of these papers, the one entitled "*Oidiomycosis of the Skin and its Fungi*" is a most comprehensive and exhaustive presentation of the subject, and occupies 157 pages in the book. This is followed by several shorter papers on additional cases of the condition and on the biology of the organism by Dr. Ricketts and his colleague Dr. B. F. Davis. A series of papers on more or less abstract points in immunology is followed by the extensive studies in Rocky Mountain spotted fever. The reader following this series of papers can trace step by step the procedures in the field and the work in laboratory and institute which led to the unravelling of the mystery of this disease. The material presented by Dr. Ricketts is admirably collated and summed up in his Carpenter Lecture before the New York Academy of Medicine, included as a part of the series. Appended are several studies on Rocky Mountain spotted fever carried out by associates of Dr. Ricketts—Drs. B. F. Davis, W. F. Peterson, J. J. Moore, M. B. Maver, and E. R. Le Count. The papers on spotted fever occupy 172 pages, and the book is concluded with the magnificent studies on the typhus fever of Mexico, during which the heroic worker sacrificed his life.

The book is well printed on heavy paper, is neatly bound in cloth, the illustrations are beautifully presented, including the frontispiece portrait, the grouping of the studies is splendid, and all in all the volume is well fitted to be the permanent memorial to a noble investigator, a man of ability and energy, a man of high ideals and "a pure love for search after the truth in his chosen field." "The torch was placed within the grasp of hands fit to carry it forward and during the few short years given him he advanced it farther than we may realize at this moment, because he broke open paths for future progress."

The medical public suffers in that the introductory address by Dr. Hektoen fails to bring the reader into intimate touch with Ricketts, the man, fails to point out those influences of childhood,

youth, and early manhood that make for that love of truth, scientific achievement, and noble character, so well exemplified in Ricketts' life. At a period when Medicine stands in great need of men such as Ricketts the inspiration of insight into the formative period of his life cannot be overestimated. Nevertheless, the address presents at some length the development of Ricketts' work after he took up active investigation, and points out clearly the great strides forward which resulted from his studies. As a eulogy the address is admirable, and its stimulation cannot fail to be far reaching.

The papers presented are too well known and too diversified to permit of criticism, even if good taste permitted it. All the studies show the painstaking thoroughness and attention to detail that mark the great investigator. The studies are rife with suggestion, and must be of great inspiration to all who read them. H. T. K.

THÉRAPEUTIQUE USUELLE DU PRACTICIEN. By ALBRET ROBIN, Professeur de Clinique Thérapeutique à la Faculté de Médecine de Paris, Membre de l'Académie de Médecine. Volume II; pp. 530. Paris: Vigot Frères, 1911.

THIS work is the second volume of an annual series, representing year by year the lectures given at the Beaujon Hospital by Professor Robin. Each year the treatment of a picked group of diseases of various types is lectured upon in great detail in the twenty-six lectures which constitute the course. The present volume is devoted to infectious diseases—typhoid, erysipelas, and rheumatism; metabolic—polyarthritis deformans, gout, and diabetes; respiratory—pneumonia, acute pulmonary edema, pleurisy, and bronchitis; nervous—cerebral softening, cerebral syphilis, and paralysis agitans; skin—prurigo.

The individual topics are fully discussed with the characteristic French fondness for ultimate classification, which, though burdensome, helps one to appreciate the gratifying exactitude of detail.

One cannot help being impressed by the emphasis laid upon certain points which in our literature do not receive much attention. As an example, over twenty pages are devoted to a discussion of the treatment of the albuminuria in diabetes with a division of the albuminuria into three types and a plan of appropriate treatment for each. However, it is in this difference of viewpoint that the value of a foreign work partly lies.

It is difficult to estimate the value of the entire series from a single volume, but it is scarcely probable that any work of this nature will become very much used outside of France. However, for pleasant reading and suggestiveness, it can be heartily recommended.

O. H. P. P.

DIAGNOSIS AND TREATMENT OF DISEASES OF WOMEN. By HARRY STURGEON CROSSEN, Professor of Clinical Gynecology, Washington University. Second Edition; pp. 1025; 744 illustrations. St. Louis: C. V. Mosby Co., 1910.

THE book contains seventeen chapters. The first three are devoted to methods of examination, diagnosis, and treatment. Then follow chapters on diseases of the external genitalia and vagina, lacerations of the pelvic floor and genital fistulæ, displacements and nutritive and inflammatory diseases of the uterus.

Malignant diseases of the uterus and fibroid tumor are considered separately. The diseases of the adnexa are discussed in three chapters: one on pelvic inflammation; one on tumors of the ovary and the parovarium; and one comprising tubal pregnancy, pelvic tuberculosis, and other minor subjects.

Malformations of the genital apparatus and disturbances of function make up Chapters XIII and XIV. Chapter XV describes the operative technique of abdominal section, vaginal section, and conservative surgical procedures.

The after treatment of operative cases is fully related in Chapter XVI, while the last chapter is entitled "Medicolegal Points in Gynecology." In an appendix to the volume, numerous formulæ are given of cathartics, emmenagogues, ointments, powders, etc., used in the practice of gynecology and pelvic surgery.

The author has endeavored to present the diagnosis and treatment of gynecological diseases as they are met in the office or at the bedside by the general practitioner. Particular and detailed attention, therefore, is given to diagnosis and the selection of operative or other treatment.

There is no doubt that the author has succeeded in his effort, for the volume is replete with diagnostic points, and the operative and supplemental methods of treatment as given need no explanation.

The book is profusely illustrated by original and borrowed pictures. These serve their purpose admirably. The original illustrations are not uniformly good from the artistic standpoint, and the appearance of familiar illustrations from other text-books is an unhappy feature.

In some places there is too much breaking of the narrative and too much tabulation for easy reading. The volume is a mine of information, creditably presented. It will be particularly valuable to the man who wishes to do gynecological work, but who has not had an opportunity to acquire much clinical experience as hospital interne or dispensary assistant.

B. M. A.

KURZGEFASSTE CHIRURGISCHE OPERATIONSLEHRE FÜR STUDIERENDE UND AERZTE. By DR. AD. OBERST, First Assistant in the Surgical Clinic and Privatdocent for Surgery in the University of Freiburg, i. Br. Pp. 198; 232 illustrations. Berlin: S. Karger, 1911.

THIS text-book for a course in operative surgery includes: (1) Incisions of the Soft Parts, their Repair by Suture, and Hemostasis; (2) Ligation of Arteries in Continuity; (3) Amputations; (4) Excisions of Joints; (5) Operations on the Head and Face; (6) On the Neck; (7) On the Thorax, Spine, and Abdominal Walls; (8) On the Abdominal Cavity, and (9) On the Urogenital System.

The illustrations are good, but not sufficiently homogeneous to render the book very attractive; some are too large, some are badly reproduced photographs, some are good pen and ink diagrams, and others are half-tone drawings. Most of the operations described are those generally approved and in use all over the world, but some might as well have been omitted. Among the latter is Macewen's method of pucker up the hernial sac into a pad, with the intention of strengthening the abdominal wall. There is no mention of the inguinal method of operation for femoral hernia, as practised by Ruggi and others, which undoubtedly offers great advantages over the classical approach from below Poupert's ligament, especially when an intestinal resection must be done. Nor is Bunge's method of amputation described, nor methods of amputation for cinematographic prosthesis (Vanghetti, Ceci, and others). On the whole, however, a sufficiently full account is given of such typical operations as can readily be done on the cadaver, or as will come within the experience of the general practitioner.

A. P. C. A.

SYPHILIS: ITS DIAGNOSIS AND TREATMENT. By F. J. LAMBKIN, Col. R. A. M. C., London. Pp. 195. New York: Wm. Wood & Co., 1911.

THIS work considers syphilis with special attention to the diagnosis and treatment, based to a large extent on the observation and experience of the author. His position has been unique in its opportunities for the study of this disease, since he has been engaged in the treatment of syphilis in the English army, both in England and in India. Moreover, for the last few years he has been in charge of the chief military hospital for venereal diseases. Syphilis, being very common among soldiers, lends itself, however, most excellently to treatment because of the system in the army enabling treatment and observation to be strictly carried out.

The writer begins his subject with a brief, but interesting historical *resumé* then passes to the pathology and clinical course of the

six syphilis periods, followed by an exhaustive contribution on the treatment in its various forms. He gives clearly and succinctly the advantages and disadvantages of each method, and rather favors the intramuscular method of administering mercury. He also writes of the modern treatments by the arylarsonates, "Hata" or "606," and points out the great advantage the Wassermann reaction is to modern physicians, both in diagnosis and as an index of the patient's condition. The subject is well covered in all its phases, practical facts emphasized, and no wasting of space on more or less groundless theories.

The diction is good, the style easy and pleasing, and the arrangement and completeness all that could be desired in a book of this size on a subject like syphilis, upon which so much work has been done.

E. L. E.

THE WASSERMANN SERODIAGNOSIS OF SYPHILIS IN ITS APPLICATION TO PSYCHIATRY. By FELIX PLAUT, M.D., Scientific Assistant in the Psychiatric Clinic of the University of Munich. Translated by SMITH ELY JELLIFFE and LOUIS CASA-MAJOR. Pp. 189. New York: Journal of Nervous and Mental Diseases Publishing Company, 1911.

THE monograph of Dr. Felix Plaut starts with a brief, clear-cut history of the experimental work that lead up to the exposition of the Wassermann reaction, and of some of the later investigation into the nature of the phenomena. He compares critically some of the main modifications of the test, concluding that the original Wassermann test with aqueous solution of syphilitic fetus as antigen is the method of choice. In a brief, suggestive, but wholly undetailed chapter, he reviews the technique, emphasizing fully the rationale of the controls.

In the main body of the book, he studies (1) Those cases of syphilis without involvement of the central nervous system, finding in the vast number of cases a positive reaction in the blood serum and in all cases, a negative reaction in the spinal fluid. The strength of the reaction is in no way parallel to the clinical findings or to the cellular content of the spinal fluid. (2) In paresis he finds a strongly positive reaction in the blood and cerebrospinal fluid. The strength of the reaction in the two fluids being generally equal and in more or less complete agreement with the cytological findings. Here again there is no parallelism between the biological tests and the clinical manifestations of the disease. The positive serological results separate paresis from post-traumatic psychosis, alcoholic pseudo-paresis, and from manic depressive states. Its importance is distinct in differentiating between beginning paresis with depression, and little or no demonstrable mental weakness, and in those other

cases, which show typical manic excitement, with at the same time suggestive signs of paralysis. Here the fact that you may be dealing with a nonlucetic psychosis in a syphilitic or in a parasymphilitic or in a non-symphilitic individual makes the formula or type of reaction in these cases all important.

These types are: (1) In paresis a strongly positive reaction in the serum and in the cerebrospinal fluid with positive cell count. (2) In cerebrospinal syphilis a positive result in blood serum, very weak or absent reaction in the cerebrospinal fluid, and a positive cell count. (3) In the psychoses attacking a syphilitic with no involvement of his nervous system a positive serum reaction only.

In the etiology of dementias of childhood, Plant thinks syphilis plays an important role. The reaction acts here exactly as it does in acquired forms.

The book is abundantly illustrated with carefully chosen cases and the painstaking balancing of clinical manifestations, cytological investigations, serological tests, and where possible anatomical studies make the book most valuable and interesting. One cannot but wish that the chapter on technique were fuller and more detailed and that in a few places the clinical facts were more condensed. The book has a poise, balance, and reserve which makes it stimulating and suggestive.

E. P. C. W.

A MANUAL OF SURGERY. By FRANCIS T. STEWART, M.D., Professor of Clinical Surgery in the Jefferson Medical College, Surgeon to the Germantown Hospital, and Out-patient Surgeon to the Pennsylvania Hospital. Second edition; pp. 682; 553 illustrations. Philadelphia: P. Blackiston's Son & Co., 1911.

THE author has afforded his readers an excellent work in this the second edition of his surgery. The book, primarily for the student, also makes an excellent work of reference for the general practitioner; both of whom have in it a manual stripped of verbiage, useless theories, and non-essentials. It is brief, practical, and sets forth in a clear, concise and well-arranged order the essential facts of present-day surgery.

Many little details of treatment and diagnosis, so often neglected by authors as being too commonplace to need description, are clearly and minutely described with especial reference to their practical application by even the beginner, as a student must necessarily be. All unnecessary historical and bibliographical references have been omitted.

Many of the illustrations are original, being made from photographs of actual cases. The text is clearly and admirably arranged with important words in italics or in heavier type, a good plan

for helping the student grasp the relative importance of the subject under discussion. A good, well-arranged index is added.

Of a necessity much that is important in many phases of the subject is omitted because of a desire to be brief. The chapter on bandages and plaster-of-Paris dressings is rather too concise, and could well be treated more fully, taking, if need be, some of the space now allotted to bacteriology, immunity, etc., subjects that a student is taught elsewhere in his course. It is a question of opinion whether gynecology should be treated as a part of general surgery, but the author has deemed it wise to insert a chapter on this subject.

Finally, the book is good enough, brief and concise enough to fill the wants of a busy student who has but little time to cull the important facts from the non-essentials, as he must necessarily do in many works on the subject of surgery. E. L. E.

PLASTER OF PARIS AND HOW TO USE IT. By MARTIN W. WARE, M.D., New York, Adjunct Attending Surgeon, Mt. Sinai Hospital. Second Edition; Pp. 100; 90 illustrations. New York: Surgery Publishing Company, 1911.

THIS work, originally based for its subject matter on ten years' experience with over 5000 dispensary cases of joint diseases and fractures, has justly received its second edition. The book fills a want for both private and dispensary surgeons.

The use of plaster of Paris is usually taken up in text-books as a minor matter, about which all should be conversant. The author presents the subject in its entirety, taking up, in order, the minutest details, explaining each detail in a clear, practical, and concise manner. He describes the preparation of plaster bandages and how they can be most economically made, a point of some importance, especially in institutions, their care and general points in their application. He takes up practically examples of all cases in which plaster might be used, and describes in detail the technique of each individual dressing, even explaining how best to pad the edges and remove spots of plaster from the floors, linen, hands, etc., a point but seldom mentioned. The advantages of the various dressings of plaster in isolated cases are discussed, and those advocated that have proved the most satisfactory in the author's wide experience.

The work is well written, important points clearly stated, and abundantly illustrated with numerous good cuts, most of which are original. With this book on one's shelf, there is no excuse for improper application of plaster on any part of the body.

E. L. E.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Paroxysmal Tachycardia.—H. E. HERING (*Münch. med. Woch.*, 1911, lviii, 1945) summarizes his clinical and experimental findings in paroxysmal tachycardia as follows: (1) With regard to the origin of cardiac stimuli in paroxysmal tachycardia, it is established that there are both auriculoventricular and pure auricular tachycardias. (2) Whether the auricular paroxysmal tachycardia, like the auriculoventricular variety, is heterotopic, has not been definitely proved, though the weight of probability seems to favor this view. (3) The stimuli causing an heterotopic paroxysmal tachycardia may be primary heterotopic or heterotopic in the sense that they differ qualitatively from native impulses or stimuli (*Ursprungsreize*), probably the former. (4) In those cases of paroxysmal tachycardia which have previously been considered as nervous the impulses can only be native. (5) That a paroxysmal tachycardia may be entirely nervous in origin is proved by the experiments in which Hering was able to produce an heterotopic auriculoventricular tachycardia of sudden onset and termination through stimulation of the accelerator during vagus tonus. (6) These experiments also lend support to the view that the stimuli causing extra systoles may be primary heterotopic stimuli, a conception which requires further confirmation, but which is adapted to the explanation of those cases of extra systole in man which are often interpreted as neurotic in origin.

Immunity of Spirochetes to Arsenic.—The experience of many workers seems to show that, in the majority of cases, a single dose of salvarsan is insufficient to produce a cure in syphilis. The tendency

at the present time is to give repeated injections of the drug. As it has been shown that other protozoa, namely, trypanosomes, may acquire an immunity to arsenical compounds, it becomes of great practical importance to know whether spirochetes are capable of developing a similar immunity. M. ROTHERMUNDT and J. DALE (*Deutsch. med. Woch.*, 1911, xxxvii, 1790) have undertaken an experimental study of this question in connection with chicken spirillosis. It seemed impracticable to study the *Spirocheta pallida* itself in experimental animals, because of the long intervals of time required to transfer the infection from one animal to another. Atoxyl and salvarsan were the preparations used. Rothermundt and Dale found that passage of the organisms through twenty chickens within a period of two months, the animals being constantly under arsenical treatment, led to no appreciable immunity to the drug on the part of the spirochetes. They therefore believe that there is little cause to fear the development of arsenic immunity on the part of the *Spirocheta pallida* in patients subjected to repeated injections of salvarsan.

The Babinski Phenomenon in Uremia.—H. CURSCHMANN (*Münch. med. Woch.*, 1911, lviii, 2054) publishes further observations upon Babinski's plantar reflex as a sign of impending uremia. Illustrative cases are described in some detail. Curschmann's experience with the test leads him to conclude that in nephritics considerable valuable information may be gained by constantly testing for the Babinski phenomenon. In threatened uremia the Babinski reflex may become positive before there is any mental disturbance or before the appearance of the preuremic increase of the tendon reflexes.

Salvarsan in Kala-azar.—A. CHRISTOMANOS (*Deutsch. med. Woch.*, 1911, xxxvii, 1705) has tried salvarsan intravenously in the treatment of kala-azar. He used it in doses of 0.007 to 0.01 grams per kilo. of body weight. There was no discernible effect on the course of the disease and no noticeable decrease in the number of parasites. The staining reactions of the organisms were also unaffected. The drug is therefore probably without value in the treatment of kala-azar.

Adrenalin and Asthma.—H. JANUSCHKE and L. POLLAK (*Arch. f. exp. Path. u. Pharm.*, 1911, lxvi, 205) have made an experimental and clinical study of the effect of adrenalin upon the bronchial musculature. It has been observed previously that adrenalin was useful in the treatment of bronchial asthma, and the present investigation was made to determine the cause of the favorable action. The experiments were performed upon dogs and cats. To produce spasm of the bronchioles, muscarin was employed. Januschke and Pollak found that intravenous injections of adrenalin caused an increase of the respiratory excursions of the lungs. The increase, however, was less noticeable in normal animals than in those suffering from "muscarin asthma." The antagonism observed between muscarin and adrenalin made it clear, furthermore, that bronchial spasm, and not embarrassment of the pulmonary circulation, was the chief factor in the production of muscarin asthma, since it was shown that the spasm was relaxed by adrenalin. Asthma produced by the injection of peptone was also relieved by adrenalin, but

that caused by B-imidazolylethylamin was unaffected. They found, too, that the bronchial dilatation which adrenalin induces was not overcome by ergotoxin. The findings reported are of interest in explaining the action of adrenalin in bronchial asthma. By the use of adrenalin injections Januschke and Pollak say it should be possible to determine to what extent bronchial constriction plays a role in the production of other forms of asthma. They have studied a few cases, and their results make it seem probable that spasm of the bronchioles is an important factor in the asthmatic attacks so often seen in cardiac and renal insufficiencies, as well as in the transient dyspneas of pulmonary emphysema. That one of the causes of transient bronchial spasm is irritation of a bronchial constrictor centre in the medulla from congestion is probable, since clamping of the superior vena cava, the vagi being intact, produced narrowing of the bronchi.

The Immediate Effects of Splenectomy on Hemolytic Jaundice.—F. MICHELI (*Wien. klin. Woch.*, 1911, xxiv, 1269) reports remarkable improvement, in fact, an apparent cure, following splenectomy in a patient with acquired hemolytic jaundice. The patient had been under observation for three years and presented all the clinical, hematological, and biological symptoms of the disease. Various forms of treatment had caused only slight temporary improvement. The icteric hue never disappeared. For three months prior to operation, the highest red count was 2,600,000, the lowest 980,000. Following splenectomy, the urine, which had been rich in urobilin, cleared almost at once, and in a few days the jaundice had entirely disappeared. The liver returned to its normal size. Likewise, the hemoglobin rose from 30 to 65 per cent., the red count from 1,800,000 to 4,000,000. The resistance of the red cells to hypotonic salt solutions, markedly lowered before the operation, now became normal, and at the same time the erythrocytes showing the reticulofilamentous substance on vital staining diminished from 25 to 50 per cent. before splenectomy to the normal proportions. About two months after the operation the patient was apparently perfectly well, and felt well for the first time in years. The spleen was found to be sterile, containing neither bacteria nor protozoa. The injection of fragments of the spleen into the peritoneal cavity of guinea-pigs caused no symptoms of disease within thirty days.

Eosinophilous Cells in the Gastric Contents in Achylia Gastrica.—S. MOACANIN (*Wien. klin. Woch.*, 1911, xxiv, 1335) has been able to find several reports where numerous eosinophile cells have been observed in the wall of the stomach post mortem in cases of carcinoma ventriculi and of achylia gastrica. Such cells, however, have not been noted previously in the gastric juice. In Moacanin's case the patient suffered with achylia gastrica and mucous colitis. Eosinophilic cells were found in the gastric contents, and also in the mucus of the stools. Since the eosinophiles may infiltrate the gastric tissues in the neighborhood of atrophying glands, it is possible that the finding of these cells may be found to be indicative of an atrophic condition of the mucosa.

Secondary Hemorrhage Following the Application of Leeches.—E. WEILL and C. NOURIQUAND (*Presse. Méd.*, No. 87, November, 1911, 881) describe, in addition to primary hemorrhage following leech applications, in certain cases a secondary hemorrhage at the site of application, developing three and one-half to five hours later, often difficult to control, and of considerable severity. They have observed this in 6 of 100 cases, in patients of varying ages and both sexes. A striking feature is that in all cases there existed an enlarged liver, with or without chronic cardiac lesions, albuminuria, and nephritis. They consider the hepatic condition of especial importance, but admit from careful analysis, that the number of leeches applied may play a part in the quickness of development, and severity of the hemorrhage. Similar observations of general hemophilia after leech applications have been made. The phenomenon seems best explained by assuming absorption of hirudine deposited by the leeches at the point of application. This may be very small in amount, but increased by the number of leeches. For experiments show that an infinitesimal quantity of hirudine in the plasma renders it anticoagulant. Weill and Nouriquand have demonstrated this *in vitro* by diluting "hirudinized serum," and testing it with 50 or 100 times its content of blood; or by adding equal amounts of calcium chloride or diphtheria toxin without coagulation. Three cubic centimeters of "hirudinized" plasma, with equal amount of the sediment after centrifugalization were injected into a guinea-pig. Twenty minutes later severe hemorrhage developed at the sites of injection, lasting for an hour and ten minutes. In three other animals similarly treated, wounds bled more freely and for a longer time than control pigs similarly incised. Weill and Nouriquand conclude that under certain conditions hemorrhage may develop after leech applications in consequence of a hemophilia due to hirudine. Investigations have been made showing that hirudine is a nucleoproteid, which they hope to demonstrate in the blood of such patients.

Deviation of Complement by the Serum of Healthy Diphtheria Bacillus Carriers in the Presence of Diphtheria Toxin.—E. CATHOIRE (*Compt. rend. Soc. de biol.*, Paris, 1911, lxxi, 315) shows that individuals are found in whose nasopharynx toxic strains of *B. diphtheriae* are growing without the least evidence of injury. Such are usually not convalescent from diphtheria; they are generally not affected by local disinfection. Cathoire has attempted to investigate the mechanism of this immunity by testing the patients' serum against diphtheria toxin on the assumption that the bacilli are pathogenic only when their toxin is able to destroy the natural defence of the organism. The method was by trying the complement-fixation reaction of the serum of such carriers in the presence of diphtheria toxin. The sera of 5 patients were considered, in whom toxic bacilli had been found in greater or less abundance for several months. Cathoire first demonstrated that the strain of toxin used did not deviate in doses of 0.5 c.c. a hemolytic system of 1 c.c. of sheep's corpuscles diluted and sensitized, activated by a sufficient quantity of fresh guinea-pig serum. He obtained sharp deviation of the complement, however, with 0.1 c.c. of toxin in the presence of carriers' serum in doses varying from 0.1 to 0.5 c.c. (the power of its hemolysis being first established).

Control, by serum of uninfected subjects showed the integrity of the complement in 9 of 10 cases. Whether in the one case a natural immunity or one acquired from previous infection was concerned the author cannot state.

Finger Phenomenon: A New Diagnostic Sign of Organic Hemiplegia.—ALFRED GORDON, (*Jour. Amer. Med. Assoc.*, 1911, lviii, 1591). The paucity of diagnostic reflex phenomena in the upper limb is striking. The need of such signs is evident in differentiating certain cerebral lesions from spinal or other changes. Gordon reports the following sign in 8 cases of complete hemiplegia: The patient's forearm is elevated. The observer's thumb is pressed against the pisiform body, especially on its radial side, taking care not to press on the extensor muscles or the dorsal surface of the wrist. The patient's fingers are seen to extend, and sometimes to spread in fan-like form. The extension sometimes involves only the last two fingers; in other cases all five. This phenomenon is not very marked in old hemiplegia with marked contracture. In 6 cases of recent hemiplegia (two to six months) this reflex was prompt. In 2 cases it was only obtained after two or three trials. For control, 15 normal patients, 4 cases of brachial palsy of poliomyelitic origin, and 3 cases of hysterical hemiplegia were tested; the reflex was negative in all. Gordon concludes that between this and Babinski's phenomenon there is an obvious analogy; that further observation in many cases for its constancy is necessary.

Brill's Symptom Complex and Typhus Fever.—G. A. FRIEDMAN (*Arch. Int. Med.*, 1911, viii, 4, 427) considers Brill's original article describing a symptom complex characterized as "an acute infectious disease of unknown origin and pathology; of short incubation period, four to five days; a period of continuous fever, accompanied by intense headache, apathy, and prostration; a profuse and extensive erythematous maculopapular eruption; all of about two weeks' duration, whereupon the fever ceases by crisis or rapid lysis, when all symptoms disappear." Brill believes the complex cannot be considered typhus. Friedman believes that the disease in question is in no way different from numbers of typhus cases observed in countries where typhus is endemic, or from sporadic cases observed in the United States and elsewhere. This he thinks is supported by a review of modern literature on typhus, with especial reference to differentiating it from other diseases by modern methods which older observers (cited by Brill) could not employ. From Friedman's own experience of three severe epidemics of typhus fever in Russia, he considers that the picture of Brill's disease is in no way different from his observations of the less severe authenticated cases of typhus, in course, symptoms, and complications. From a review of the epidemiology of typhus, he believes that in many parts of the world the disease is endemic, and may be present for a long time without leading to an epidemic, and that its mortality has considerably decreased wherever good ventilation, abundance of light, and good hygienic conditions exist. Both clinical and experimental observations suggest that lice transmit typhus. If this be provisionally accepted, it throws additional light on the apparent immunity of Brill's ward patients to infection from neighbors

suffering with his disease. For it is well known that lice require more intimate contact than proximity for migration. He concludes that Brill's symptom complex is identical with moderate and mild typhus, and that, as in the far East a corresponding type is called "Manchurian Typhus," so this should not be spoken of as "a disease of unknown origin," but rather as New York Typhus, thus calling the attention of physicians to the clinical picture concerned, and not connoting something rare and unusual.

Vincent's Angina.—EDWIN H. PLACE (*Boston Med. and Surg. Jour.*, 1911, clxv, 720) briefly reviews the literature concerning both the clinical and bacteriological manifestations of this disease, and then considers its general character in the view of over 80 cases seen by himself. The onset is insidious, symptoms varying from trifling to moderate fever; malaise; sore-throat, rarely severe; foulness of breath, and bad taste in the mouth. Often the subjective symptoms are slight. The lesion may be anywhere on the buccal mucous membrane, usually involving the tonsils, and adjacent posterior pillar of the fauces and edge of the uvula. The gums may be affected, or the nose. Place has not seen a case of skin involvement. The lesion consists of a shallow ulcer with sharp cut edges, filled flush with granular cheesy material, colored white, yellow, or green, and on removal foul. Beneath it is a bleeding irregular surface. There is usually an accompanying cervical adenitis, though if marked, due to a complicating infection. The progress may be rapid, with ulceration and destruction of the tonsil. It is usually slower, tending to recover in days or weeks. In Place's experience (differing from other observers) transmissibility of the disease is not noticeable. He attributes its prevalence in asylums rather to the poor dental and oral hygiene. The lesion differs from diphtheria in being primarily an ulceromembranous process. The presence of marked edema and diffuse redness speaks against Vincent's angina. In any case, cultures should be taken. From syphilis, its lack of infiltration, general glandular enlargement, and its course make differentiation possible. From other mouth ulcerations it differs in smear, culture, course, and history. Place has made a considerable number of smear examinations, finding typical organisms only rarely, and in small numbers. Its relation to noma is interesting. In 7 cases of the latter, typical bacilli and spirochetæ were found. The earliest lesion of noma was invariably indistinguishable from Vincent's angina. That the lesion has a specific etiology is suggested from the numbers of characteristic organisms found in typical lesions, disappearing as healing begins; and from the constancy of the clinical and bacteriological pictures. The organism is a long bacillus (4 to 14 μ long by 0.5 μ thick) with tapering edges, staining best with methyl violet, and usually giving an irregularly vacuolated appearance. It is motile, and strictly anaërobic, requiring media rich in animal albumin. The accompanying spirochetes are 6 to 20 μ long, less than 0.5 μ wide, with wide curves. The relation between bacillus and spirochetes is unsettled. The most satisfactory treatment consists in swabbing the ulcer with 100 to 50 per cent. hydrogen peroxide until clean, and painting daily with 2 per cent. chromic acid. Cure usually occurs rapidly.

SURGERY

 UNDER THE CHARGE OF

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The Pathogenesis of Renal Tuberculosis According to Observations on Two Autopsy Cases.—HERESCO and CEALIC (*Ann. d. mal. d. org. gén.-urin.*, 1911, ii, 1441) report two cases with autopsies, one patient dying after operation. In both cases one lung and the opposite kidney were involved by the tuberculosis, cavities being present in the affected lungs and kidneys. There were no adhesions between the visceral and diaphragmatic pleuræ, nor was there any involvement of the mediastinal or aortic lymph nodes, macroscopically or microscopically. In the first case there were found bacillary lesions of other organs, kidney, ureter, bladder, lungs, epididymis, and hip-joint. These facts seem to show that the path of propagation is by the blood, rather than by the lymph. Tendeloo has two cases in which autopsies were performed. In the first there were bacillary lesions of the lungs and tracheobronchial lymph nodes; adhesions between the right visceral and diaphragmatic pleuræ; bacillary lesions in the upper end of the right ureter; and a caseous node on the anterior surface of the vena cava. In the second case there was an enlarged and painful tracheobronchial lymph node, adhesions between the base of the right lung, the diaphragm, and the liver. The aortic nodes and those of the right renal vein were enlarged and caseous. From these two autopsies, Brongersma concluded that the primary infection is of the lung or the mediastinal nodes, and from there it is propagated by the lymph paths to the kidneys. The two cases reported by Heresco and Cealic demonstrate the opposite view, that the propagation is hematogenous.

The Cure of Prostatic Obstruction.—YOUNG (*Surg., Gynec., and Obstet.*, 1911, xiii, 269) says that his first operations on the prostate, were by the suprapubic route, by which he has operated on 45 cases with a mortality of about 10 per cent. He has done the Bottini operation in 85 cases, but has abandoned it and is using the perineal route, with which his mortality has been about 3 per cent. During recent years he has operated on about 70 cases, in which neither the suprapubic nor perineal prostatectomy were suitable, by a new method—the urethrosopic median bar excision by means of a special “punch.” He has had in all about 700 cases, on which he has done one or the

other operation. That radical removal of a carcinomatous prostate can be done through the perineum is shown by the fact that Young has 2 cases alive and apparently well, 1 after six years, and the other case after one year. Perhaps one of the greatest advantages of the perineal operation, as Young performs it, is that after enucleation of the prostate, there exist two lateral extravescical cavities, which can easily be packed with gauze, thus completely stopping the hemorrhage, cavities which rapidly collapse after removal of the gauze on the following day, and which do not form intravesical pouches of suppuration. Another great advantage is that the patient can be up in a wheel chair within two or three days, with splendid dependent drainage. The absence of any case of death from sepsis and the remarkable freedom from lung complications is shown in a series of 450 cases of conservative perineal prostatectomy.

Anesthetization of the Brachial Plexus.—KULENKAMPFF (*Zentralbl. f. Chir.*, 1911, xxxviii, 1337) says that Hirschel's communication on anesthetization of the brachial plexus has led him to report on his own attempts in this direction. The brachial plexus corresponds approximately to the middle of the clavicle. Here, even in fat people, it lies close under the surface, and its cords lie close together. The area to which the needle must pass, is bounded internally by the easily detected subclavian artery, externally by the clavicle and below by the first rib. The nerves lie between the scalenus anticus and medius, where they are surrounded by loose connective tissue, in which fluid easily infiltrates, so that a small quantity of the anesthetic injection will give an extensive effect. The technique was developed on Kulenkampff himself and in operations on his patients. The patient occupies a sitting position, and the subclavian artery is located by its pulsation, which can often be seen with the head in certain positions. It lies almost always where a continuation of the external jugular vein strikes the clavicle. The point of insertion of the needle is just external to this, close upon the upper edge of the clavicle. A fine hollow needle, about 4 cm. long, is made to penetrate almost to the first rib and to seek one of the nerves, when a paresthesia radiates to the arm, and there are seen signs of motor irritation; but there is no pain, as Kulenkampff observed on himself. If the direction of the needle is correct, this paresthesia develops as soon as the skin, superficial and deep fascia are penetrated. The injection of the fluid should be avoided until the paræsthesia occurs in the arm, because it will eliminate the tenderness, and thus render difficult or impossible exact exploration. The needle should be directed somewhat inward, backward and downward, in the direction of the second or third dorsal spine. The plexus is about 3 cm. deep, the first rib a little deeper. If the rib is struck without the plexus being met with, it will be because fear of the subclavian artery has caused the needle to pass too far outward. The needle must then be tried successively farther inward, until the paresthesia is obtained. In adults, 10 c.c. of a 2 per cent. novocain-adrenalin solution, with the usual percentage of the latter drug, should be injected. In children, 5 c.c. will be sufficient. As a rule, in from fifteen to twenty minutes the anesthesia is present and involves the whole arm, except for a triangular area over the deltoid. There is also a severe paresis of the whole arm, and a part of the shoulder muscles. The anesthesia lasts

usually from one-half to two or three hours. The method was tried on 25 cases. In 23 a tourniquet was applied to the upper arm without giving the slightest distress. In 1 the tourniquet was removed at the end of an hour because of pain. In 2 cases it was not necessary, and the anesthesia was complete. In 3 cases a few cubic centimeters of ether were necessary. In 15 cases a total anesthesia with a partial paralysis of the arm was obtained. A sufficient hypcsthesia in some parts and a complete anesthesia in others were obtained in 5 cases. In 5 others some regions were anesthetic. In a third of the cases the anesthesia did not extend to the region supplied by the supraclavicular and the intercostohumeral nerves. This can easily be overcome by a circular injection of the arm. The method is applicable to all operations on the arm up to the shoulder-joint.

The Treatment of the Duodenal Stump in the Billroth II Method of Resection of the Pylorus.—SCHWARZ (*Zentralbl. f. Chir.*, 1911, xxxviii, 1402) says that while the Billroth II method of pyloric resection has the unquestionable advantage that the divided ends of the duodenum and stomach are not exposed to the same tension at the line of sutures as in the Billroth I method, it has a disadvantage in the insecurity of the duodenal closure. A fatal termination often results from fistula formation, suppuration, and peritonitis. For this reason Brunner sutured the duodenal stump into the abdominal wall. Steinthal covered it with omentum and a gauze tampon. Kausch regarded this danger so seriously that he gave up entirely the Billroth II method (closure of the gastric and duodenal stumps with a gastro-enterostomy) and preferred the Billroth I method (end-to-end suture of the duodenal and gastric stumps). There is evidently no reliable, primary method of closing the duodenal stump. Schwarz believes that he has a simple method which serves the purpose. The difficulty in closing the duodenum securely lies in the fact that the posterior wall is not completely covered with peritoneum, so the closure by a Lembert suture is impossible or only incompletely so. Schwarz employs the following method: Pylorusward from the clamp grasping the duodenum he introduces a careful, continuous occlusion suture, taking in all of the layers. The clamp is then removed and the edges of the peritoneum brought together behind the duodenum by a continuous, superficial suture for at least 3 cm. The portion of the duodenum involved in the operation is then completely surrounded by peritoneum. Then follows a purse-string suture catching the peritoneum. Before tying this suture, the end of the duodenum with the first line of sutures (for occlusion) is pressed into the duodenum. After tying the purse string there will be a complete closure, and there will be no necessity for the aid of the omentum, for drainage or a tampon.

A New Method of Re-uniting the Divided Ureter.—FORSSEL (*Zentralbl. f. Chir.*, 1911, xxxviii, 1369) says that in the removal of a large retroperitoneal fibromyoma, he divided the left ureter where it lay in a groove in the tumor, and pulled the ureter out of the pelvis with the tumor. As he had no confidence in the methods of treating this condition, he devised one at the time. He concluded to pass the upper divided end into the lower, and in order to be able to remove

a sufficient portion of the mucosa of the lower end for contact with the external surface of the upper end, he divided the lower stump longitudinally about 1 cm. from the end. The mucosa was then removed for about 0.5 cm., which was not difficult, with the proper fixation of the ureter. The renal end was then drawn into the vesical end by means of a mattress suture of catgut, which was introduced through the whole wall a few millimeters from the end of each stump, directly opposite the longitudinal incision, the sutures being tied on the outside of the lower stump. The longitudinal incision was then closed by two catgut sutures, and the transverse margin of the lower stump was sutured to the outer layer of the upper stump. A tampon was placed to prevent urinary extravasation, but it was not necessary and was soon removed. Almost two years later, it was established by ureteral catheterization that the urine came out of the left ureter rhythmically, and that the catheter passed without any signs of resistance at the site of the wound in the ureter. A search of the literature showed that Gubaroff had done a similar operation, but without removal of the mucous membrane. Death of the patient on the thirty-first day had no relation to the operation. A postmortem showed complete restitution of the ureter. Pozzi did an operation in which he tried to bring the connective-tissue surfaces together, but four or five months later a stricture was found in the ureter at the site of the operation. Forssell thinks that this operation is to be preferred to all others, when it can be carried out, because of its simplicity; because it provides immediately at the site of the wound a good hindrance to the escape of urine; it is well suited for a quick and safe adhesion of the apposed ends of the ureter; it makes only a small sacrifice of the length of the ureter; and it does not sacrifice the normal opening of the ureter into the bladder.

A Contribution on the Employment of the Tubular Speculum in Laparotomies.—NYSTRÖM (*Zentralbl. f. Chir.*, 1911, xxxviii, 1403) says, in connection with Kuhn's recent contribution on this method in the *Zentralblatt*, that Gårdland, of Stockholm, has been using for two years in cases of peritonitis, a rectal speculum, very similar to the instrument employed by Kuhn, and has been using it in the same manner for obtaining a deep view of the peritoneal cavity through a small incision in the abdominal wall. Nyström has been employing a modification of the usual tubular rectal speculum. The rounded end of the obturator fitting into the speculum is made of glass, and is carried to the bottom of the speculum by a narrow handle, which permits a view through the glass end when it is in position. The usual electric lamp can be employed for light. Through this glass window at the end of the speculum the introduction of the instrument can be controlled. Nyström is more conservative than Kuhn as to the availability of the instrument for a complete examination of the abdominal cavity. Omentum and mesentery can so obstruct the speculum as to make it difficult or impossible to see some parts of the abdomen. In one case with symptoms of peritonitis, which was at first taken to be one of cholecystitis, a small abdominal incision was made along the right costal margin, and the speculum introduced. The upper part of the abdomen could be rather easily examined, but no focus for the

peritonitis could be found, as the peritoncum was everywhere smooth and shining and showed no exudate. Then the speculum was passed to the middle and lower parts of the abdomen, but no exudate could be seen here, nor could the appendix or cecum be seen. Only after enlarging the wound and introducing the finger, was there found an infiltration behind the upper part of the ascending colon. Through an incision at a suitable place a gangrenous appendix with abscess was exposed and extirpated. With more experience, its usefulness will be increased and its limitations become better known. Even without a specially developed technique it is very serviceable. Several weeks before the reading of his paper, Nyström operated on a case of fracture of the pelvis with symptoms of rupture of the bladder, supposed to be on the anterior side. The prevesical space was opened by a median incision above the symphysis, and in the wound was found a considerable infiltration of urine. With the finger there was felt deeply a suspected place of rupture. With a small rectal speculum, without further enlargement of the wound, there was seen a small rupture, and through the speculum a Nélaton catheter was passed into the bladder. In order to exclude an intraperitoneal rupture, an incision was made in the peritoneum close to the bladder, wide enough only to pass the speculum. The posterior wall of the bladder and surrounding parts were examined. In the neighboring intestine and mesentery were found small hematomata, but the bladder wall was smooth and free of peritoneal irritation and exudate.

Concerning the Circular Suture of Vessels, Arteriovenous Anastomosis, and the Transplantation of Vessels.—YAMANOÛCHI (*Deut. Zeit. f. Chir.*, 1911, cxii, 1) made an experimental study of bloodvessel suture, his observations being based upon 117 operations of various kinds. He says that arteries and veins divided transversely can be reunited very successfully. The healing at the line of sutures takes place by connective tissue, in which a part of the elements of the vessel wall is preserved in the line of union. The failures in circular suture are due to defects in the technique. For the filling in of an arterial defect from resection, a piece of vessel from the same individual is best suited. The transplanted vessel, whether artery or vein, lives permanently. If a vein is employed, it soon withstands the arterial blood pressure, because its wall increases in thickness. The healing at the line of sutures results from new tissue formed from the implanted and original vessel stumps, as well as from the perivascular tissue. The autoplasmic implantation of a piece of vein into an artery is to be recommended as a surgical procedure, since the vein, even if it is larger, can be resected, as a rule, without noteworthy disturbances. It is possible to transplant a piece of vessel into an arterial defect of another individual of the same or another species. The transplanted vessel, however, slowly disappears, and is substituted by the body tissues, so that finally it is surrounded by a connective-tissue tube, which is coated internally by epithelium developed from the ends of the stumps of the body vessel. The healing at the line of sutures takes place merely by growth from the body tissues, while the transplanted vessel remains wholly passive. In practice this method is not suitable, because dangerous complications may result, such as secondary

hemorrhages and aneurysmal formation. Portions of arteries from recently dead animals of the same species may be transplanted successfully. Histologically and practically, the process is the same as in the above. It is also possible to transplant successfully portions of vessels, preserved in Lock's solution, physiological saline solution, or sterile water at a temperature of 0° to 1° C. The preserved vessels before transplantation show no noteworthy histological changes. Whether it lives or not has not yet been established. At any rate, after transplantation, according to the individual differences, it will be slowly resorbed and substituted by the body tissues. Finally, even dead portions of vessel may be transplanted with success. This is an interesting experiment, physiologically, since it shows that the presence of living vessel epithelium is not absolutely necessary to prevent intravascular thrombosis. Circular arteriovenous anastomosis is an operation which is easily carried out. The blood afterward flows peripheralward, while the resistance of the valves disappears. The question whether the blood flows back through the capillaries to the heart or through the anastomosis with the vein, is not yet solved.

Fibro-epithelial Tumors of the Mammary Gland.—GREENOUGH and SIMMONS (*Annals of Surgery*, 1911, liv, 517) say that a comparative study of the fibro-epithelial tumors of the breast shows that their relations one to another are very close, and justifies their being grouped together as in the Warren classification. The essential features of the tumors of the fibrous types is the presence of periductal fibrous tissue in more or less abundance about the gland ducts. This periductal fibrous tissue may vary in cell richness from normal fibrous tissue to myxomatous or sarcomatous tissue. The two types of tumor, however, with this exception, are so much alike that the sarcoma type may be well considered merely a modification of the benign fibroma. The periductal fibroma needs only excision of the tumor to effect a cure. For the periductal myxosarcoma, amputation of the breast is advised, without removal of the muscles or dissection of the axilla; the tumor is only locally malignant. The fibrocystadenoma group includes a few tumors of similar origin to the foregoing, which display, when examined by the microscope, a tendency to epithelial overgrowth. The diagnosis between fibrocystadenoma and periductal fibroma cannot be made with certainty before the removal of the tumor. This tendency to epithelial proliferation is encountered in other diseases of the breast, such as abnormal involution of cystic disease; and is an undoubted source of danger to the patient in adult life. For this reason complete removal of any fibro-epithelial tumor of the breast by early operation is the best treatment to be advised.

On Impacted Fracture Through and Near the Femoral Neck.—COPE (*Annals of Surgery*, 1911, liv, 682) says that impacted fracture of the neck of the femur (within the capsule) is by no means an uncommon occurrence. It results from direct violence applied over the trochanter major, and may permit of considerable voluntary and passive movement of the hip without crepitus. An unimpacted fracture resulting from indirect violence may occasionally be converted into an impacted fracture owing to an immediately subsequent fall upon the

affected hip. The impaction may cause an atypical deformity, even sometimes simulating a dorsal dislocation. Fracture of the base of the neck is always primarily impacted; if the force applied is great, there are always secondary fractures, both horizontal and vertical, through the trochanter region. Persons with impacted fractures of the femoral neck or base of the neck may and often do walk about for some days after the accident. An impacted fracture of the base of the femoral neck may exist without appreciable shortening when the force is not sufficient to cause the trochanter region to be split up by the wedge-like cervix femoris.

THERAPEUTICS

UNDER THE CHARGE OF

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The Action of Iron and Arsenic as Remedies for Chlorosis.—ZWETKOFF (*Zeitschrift f. Exper. Path. und Therap.*, 1911, ix, 393) compares the results obtained by the treatment of chlorosis with iron and arsenic alone with those obtained by treatment with iron and arsenic combined. The conclusions are as follows: The treatment of chlorosis with arsenic in the form of arsenous acid, either given by mouth or subcutaneously, does not result in an increase of the hemoglobin or of the number of red blood cells. The action of arsenic in chlorosis is in direct opposition to its effects in pernicious anemia. In the later disease the arsenic treatment is of the highest value. This difference of action of arsenic in these two diseases of the blood-forming organs is dependent upon some difference in the nature of the two diseases. The treatment of chlorosis with iron in the form of Bland's pills results in a rapid increase of the hemoglobin and when the blood cells are diminished an increase in their number. This regeneration of the hemoglobin and of the red blood cells is not rapid as measured by the single weeks. The treatment of chlorosis with iron and arsenic combined gives a definitely increased improvement in comparison to the results obtained by the treatment of chlorosis with iron alone. The increase of the hemoglobin occurs more rapidly, and the number of red blood cells shows an increase of two or three times that obtained when iron alone is used. The arsenic is given in the form of arsenous acid, in doses of from 0.002 to 0.003 gram three times a day. These doses are combined with the ordinary doses of iron. Zwetkoff believes that the increased benefits derived from this combination of iron and arsenic is not only a question of the added action of arsenic to iron, but that it is to be explained on the ground that arsenic directly stimulates the bone marrow, that is being coincidentally supplied with iron, to increased blood production.

Digitalis.—MACKENZIE (*Heart*, 1911, ii, 273), in a long article, reports 43 cases of various cardiac affections treated with digitalis. Each case is presented with a wealth of clinical details regarding, particularly, the effects produced by the administration of digitalis. Mackenzie draws the following conclusions from his detailed study of these cases: The careful analysis of the symptoms of patients to whom digitalis has been administered brings out the fact that individuals react differently to the drug. So far as the heart is concerned, the difference is partly dependent on the nature of the lesion with which the heart is affected. Patients with auricular fibrillation are more readily and more markedly affected than patients with the normal rhythm. Digitalis, in a proportion of patients with normal rhythm, affects the auriculoventricular bundle more particularly, producing partial heart block. It is suggested that the susceptibility of patients with auricular fibrillation may result from the tendency of digitalis to affect the bundle, the change in the auricular condition rendering the bundle more susceptible to the influence of the digitalis. It is possible that in slowing the heart's rate the digitalis acts by stimulating the vagus nerve. Digitalis tends to induce auricular fibrillation. In two cases of tachycardia, arising from an abnormal source, digitalis caused the heart to revert to a normal rhythm, first inducing fibrillation of the auricle. The diuretic effects of digitalis may be produced with no perceptible change in the heart.

Clinical Observations on the Physiological and Therapeutic Action of Large Doses of Radium Emanation.—VON NOORDEN and FALTA (*Med. Klinik*, 1911, vii, 1487) believe that large doses of radium are only indicated in certain forms of acute articular rheumatism in which both large doses and prolonged sittings seem to be most efficient. In all other diseases v. Noorden and Falta advise beginning with small doses and then gradually increasing them. Large doses of radium should be given to nervous patients only with the greatest caution. They believe that radium has a profound effect upon the body metabolism, and cite their findings to support this view. In their opinion treatment by radium emanations is best carried out in institutions, since a strict régime and care as to details of the treatment aid its beneficial effects. It is probable that many of the beneficial effects obtained at certain spas may be explained by the baths containing more or less radium in its natural state.

The Action of Heart Remedies.—LA FRANCA (*Zeit. f. Exper. Path. und Therap.*, 1911, ix, 427) from his own experimental and clinical observations has formulated the therapeutic action of various heart remedies in relation to their effects upon the irritability, conductivity and contractility of the heart muscle. He says that contractility of the cardiac muscle is increased by digitalis, spartein, convallaria and cactus grandiflora. On the other hand, strychnine, caffeine, sodium bromide and sodium iodide have no influence upon this property of the cardiac muscle. The irritability of the heart muscle is lessened by both digitalis and cactus. The irritability and the conductivity are both increased by convallaria, strychnine, caffeine, sodium bromide and sodium iodide.

The Diuretic Action of the Amino-acids.—GLAESSNER (*Therap. Monatshefte*, 1911, xxv, 479) says that glycocoll has a marked diuretic action in cases where there is passive congestion due to hepatic or cardiac disease. This diuretic effect is also observed in many cases of renal disease, but is not nearly so marked. Cases of liver disease with diminished output of urine are most remarkably influenced by the action of the remedy. Better results are obtained with glycocoll in dropsy due to cardiac incompetence if the remedy is combined with cardiac stimulants. The diuresis resulting from the action of glycocoll consists not only of an increase of water excreted, but there is also an increase in the solids of the urine. The specific gravity of the urine is increased, the amount of urea and the chlorides are higher. Glaessner says that glycocoll is an entirely harmless remedy, and it is not unpleasant to take. The usual dose given by the author is 5 grams a day. The only disadvantage of the remedy is that it is more expensive than other diuretics.

The Treatment of Hemoptysis with Digitalis.—LOCKE (*Therapie d. Gegenwart*, 1911, lii, 396) discusses the etiology of hemoptysis and points out that it may result from a number of causes other than tuberculosis. Among the most important of these causes he mentions anemia, arteriosclerosis, bronchial asthma, and acute catarrhal bronchitis. In many of these patients the hemorrhage is due to a local congestion that favors diapedesis. Locke believes that the treatment should aim to reduce this local congestion, and for this purpose he recommends digitalis. He has had good results with this plan of treatment, but emphasizes the fact that an accurate diagnosis of the condition causing the hemorrhage is necessary before the treatment is instituted.

The Effect of the Digestive Secretions upon the Activity of Digitalis and Allied Drugs.—HALE (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1515) relates a series of experiments undertaken to determine the effect of the digestive secretions upon the activity of digitalis preparations and strophanthus. He found that the acid of the gastric secretion invariably causes some diminution in the action of the glucosides of digitalis and strophanthus. He does not believe, however, that an exact determination of the degree of decomposition in practice can be made, for in all probability the rate is somewhat more rapid under actual conditions, owing to the motility of the stomach and the comparatively greater dilution of the glucosides. The rate of deterioration, however, appears to be about the same for the various glucosides, about 25 to 35 per cent. in three hours, so that this fact need not be taken into consideration in therapeutics. The further factor, however, of the action of the decomposition products of these glucosides must be considered, and it is possible that certain of the untoward effects of digitalis medication may be due to them. At any rate, in so far as is possible, it would seem advisable to prevent such decomposition, and it is suggested that this might be done by requiring the official galenical preparations to be neutral, and in practice, by prescribing an alkali along with digitalis. Ignoring the specific irritant action of these bodies on the intestinal tract also, it would seem advisable that the drug should be given

between, rather than at meals, when the gastric acidity is at the maximum, and such a procedure might possibly not cause undue irritation if a large quantity of fluid were taken at the same time.

The Use of Hypodermics of Citrate of Iron in the Secondary Anemia of Tuberculosis.—BULLOCK and PETERS (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1428) recommend highly the subcutaneous injections of citrate of iron for the treatment of secondary anemia of tuberculosis. This remedy has been employed in 256 cases, and it has not failed to improve the blood in a single case. Over 70 per cent. of these patients were in advanced and far advanced classes. The subcutaneous injection of iron citrate is a common practice with Italian physicians, and Bullock and Peters advise the use of the Italian preparations because they are less irritating locally. The dosage employed is 0.05 gram injected daily until the blood examination shows a normal condition. In most cases it required but thirty to forty injections to attain this result.

The Effects of Hypodermic Injection on the Secondary Anemia of Chronic Pulmonary Tuberculosis.—BARLOW and CUNNINGHAM (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1435) used subcutaneous injections of cacodylate of iron, sodium cacodylate and arsacetin for the treatment of secondary anemia in pulmonary tuberculosis. Twenty-eight patients were treated, and the tabulated results are recorded and compared with patients not receiving the treatment. They also give the indications and contraindications for the treatment in detail, and the choice of preparation for the individual case. They believe that the following conclusions regarding the treatment are profitable. The subcutaneous or intramuscular injection of sterile solutions of arsenic or iron, or of the two in organic combination, is entirely practicable in the treatment of the tuberculous in sanatoriums. The effects of such medication are seen chiefly in the changes in the blood and in the body weight. The preparations of iron seem to affect the hemoglobin content more profoundly than it does the number of red blood cells. The preparations of sodium cacodylate and of atoxyl (arsacetin) seem to affect the number of red cells more markedly than the hemoglobin. These solutions are in no sense specifics against the tubercle bacillus, but seem to exert a general tonic or alterative action within the organism. The use of these preparations is entirely safe, and is not attended with danger to the patient, even when continued over a period of many months. Relatively larger doses are borne when given thus than are tolerated when given by the mouth. The dosage is capable of exact control, and the amount of the drug absorbed is known definitely. The body weight is more rapidly and more certainly raised when these preparations are employed than when the unassisted, hygienic, dietetic form of treatment is maintained. There is no demonstrable increased liability to pulmonary hemorrhage accompanying the use of these preparations in pulmonary tuberculosis, even with advanced cases, and in the presence of progressive destruction of the lung.

PEDIATRICS

UNDER THE CHARGE OF

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The Vasoneurotic Symptom Complex in Children.—FRANZ HAMBURGER (*Münch. med. Woch.*, 1911, lviii, 2201) thinks that too little attention has been paid to vasomotor changes in the *neurasthenias* of childhood, although in adults it is known that arteriosclerosis and functional changes in the heart are associated with and follow *neurasthenia*. In nervous children many different symptoms are found, all of which can be traced back to an irritability in the innervation of the circulatory system, and of its chief organ, the heart. The symptoms are subjective, relating to the heart, and objective, relating to the vessels. Under the former are found palpitation, unpleasant sensation in the precordium, such as a "stitch," and a feeling of oppression. Palpitation occurs after physical exertion and to a less degree after psychological disturbances. In marked cases more or less pain and dyspnea may occur, and even symptoms comparable to the *angina pectoris* of adult life. These symptoms are, however, rare in comparison to palpitation. Objectively there is found a heaving, somewhat diffused apex beat, and slight epigastric pulsation. The boundaries of the heart are normal, or but slightly increased, the sounds are clear. The epigastric pulsation is due to the descending aorta, and not to the right ventricle, in Hamburger's opinion. The sensitiveness of the pulse is shown, on the one hand, by a rapid increase in the rate on sitting up, standing and on slight physical exertion, and on the other hand, by a *pulsus irregularis respiratorius*, increasing with inspiration and diminishing with expiration. This symptom is most marked in severe cases, but also occurs in normal children. Among the subjective circulatory symptoms are headache, similar in onset to migraine, but involving both sides of the head, usually in the occipital region. Sudden local anemias of the brain cause dizziness and unconsciousness, these symptoms and the headache being due not to a general anemia, as is often supposed, but to changes in the vasomotor system. A tendency to cold hands and feet is another symptom of this class, and also the above-mentioned cardiac pains, due, according to Nothnagel, to an ischemia of the heart muscle. Among the objective circulatory signs are noted flushing or paling on psychical disturbance, coldness of the extremities, dermatographia, visible pulsation of the carotids, and increased tension of the arterial walls in the radial and temporal arteries. Many forms of bronchial asthma probably belong to this class. There are, besides, a large number of symptoms occurring in combination, all of which can be traced back to a nervous irritability of the whole circulatory apparatus. This "*vasoneurosis*" is by far the most prominent and important manifestation of nervousness in later childhood (seven to fourteen years), and occurs also in younger children.

The rigidity of the arterial walls in nervousness is marked in many cases, and generally all children with apparently "thickened" arteries are nervous. Normally, under six years, the pulse only, and not the arterial wall, is felt by the fingers; and not until the tenth year are the arterial walls frequently palpable. Pallor, especially in school children, is often construed to be an anemia, whereas it is arterial contraction due to nervousness; such children commonly have dark rings under the eyes. Marked vasoneurotic symptoms do not usually begin until about the seventh year, when the child begins to attend school. As etiological factors, Hamburger attributes an inherited disposition and certain psychical and physical irritating or stimulating influences, such as fright and joy and autosuggestion on the one hand, and toxins on the other. The prognosis of the vasoneurotic condition is good if the psychical causes can be discovered and avoided, and the child's disposition modified by good hygiene and intelligent mental training.

The Blood Pressure in Diphtheria.—J. D. ROLLESTON (*Brit. Jour. Child. Dis.*, 1911, viii, 28) studied the blood pressure in 179 cases of diphtheria. The systolic pressure as measured by the disappearance of the radial pulse was alone taken into consideration, and the instrument was C. J. Martin's modification of the Riva-Rocci instrument. The pressure was taken daily in each case for from three to eight weeks, depending on the severity of the case. All the cases except 15 were children below the age of fifteen years. The maximum blood pressure of normal children, according to Seiler, who used the Riva-Rocci instrument, is 75 to 80 mm. from two to three years; 79 to 90 mm. from four to five years. Cook and Briggs found slightly higher figures with their modification of the Riva-Rocci, and place them at 75 to 90 mm. up to two years, and 90 to 110 mm. after two years. Of the 179 cases observed by Rolleston, 63, or 35.1 per cent. according to Cook and Briggs's estimate, and 45, or 25.1 per cent. according to Seiler's figures, showed for varying periods a pressure below the normal. The varying degrees of depression bore a direct relation to the severity of the attack, being pronounced in severe and slight in mild cases. In the very severe class, of 22 cases, 18 according to Cook, and 17 according to Seiler, showed from 5 to 45 mm. below normal. The fall in pressure occurred rapidly and steeply, there being at times 10 mm. difference between the morning and evening readings. A difference of the reading of the two wrists indicated a grave prognosis. The severe and the moderate class of cases showed a considerable fall, but less marked than in the very severe class; the severe class showing 25 and 16 cases respectively, with falls of from 3 to 24 mm., and the moderate class 11 and 6 cases respectively, showing a fall of from 1 to 14 mm. The greatest difference registered was in one case, and amounted to 38 mm. The moderate class showed the least fall from normal. The occurrence of comparatively high pressures during the first week is due to febrile disturbance before the toxins had taken effect. The preponderance of the lowest readings in the second week accords with the fact that vasomotor paralysis occurs most frequently during this period. In 2 neurotic sisters, aged seven and nine years respectively, the readings ranged between 130 and 148 mm. Hg for a month. The lowest reading in a case which recovered was 60 mm. in a girl aged

three years. In the great majority of cases normal tension was regained by the end of the seventh week. As a rule, the pulse rate followed the degree of blood pressure. Out of 103 cases in whom comparison was made between the recumbent and the erect position, in 48 the readings were the same, and in 32 the recumbent readings were higher than the erect. In only 23 was the normal relation found. This reversal is liable to occur in convalescence from any acute disease. This indicates that the resumption of muscular work should be gradual in patients showing this phenomenon of effort hypotension. The increase of blood pressure was marked in the laryngeal cases, tracheotomy being followed by a considerable fall in pressure. Early serum rashes caused no increased pressure. Late serum disturbances after the second week showed a raised pressure in 40 per cent. of cases. The onset of albuminuria usually is accompanied by a fall in the blood pressure. This is exactly opposite from its effect in scarlet fever. Any change of blood pressure occurring with early palsies were in a downward direction. During late palsies a fall was most exceptional. The estimation of blood pressure is not indispensable in forming the prognosis in diphtheria, the fatal termination being indicated by the characteristic features before the blood pressure had shown the evidence of depression. Favorable results are often found in severe cases by administration of 10-minim doses of a 1 to 1000 solution of adrenalin every two to four hours.

OBSTETRICS

UNDER THE CHARGE OF

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Puerperal Infections.—POLAK (*Amer. Jour. of Obstet.*, September, 1911) concludes that curetting, douches and examinations during the acute stage of puerperal infection break down the natural barriers and further increase sepsis, the danger increasing as the period of pregnancy advances. In acute sepsis neither the endometrium nor the placental site should be curetted in cases of acute streptococcic infection. The instrumental emptying of the uterus should not be done after eight weeks pregnancy. The best of all methods consists in digital exploration and emptying in these cases. After the uterus is thoroughly emptied the pelvis should be left undisturbed except for posterior drainage, and treatment should be addressed to improving the patient's general condition. If examination shows that the blood stream is sterile, with a leukocytic resistance, the prognosis is favorable. A local exudative focus in a puerperal patient should never be disturbed so long as the patient gains. Should pus form, the collection should be opened by extraperitoneal incision. Pelvic peritonitis, with exudate, often follows endometritis which has been neglected or improperly treated. Thrombophlebitis must be considered as a

conservative process, and care should be taken not to disturb it. In the majority of cases the natural power of resistance of the patient is localized and circumscribed, the infection ultimately destroying it. It is possible for enormous abdominal exudates to disappear without operation, and even when the tubes and ovaries are involved they may recover spontaneously. No operation should be undertaken during the acute stage of infection, and vaccines may be given to advantage in some cases.

Decapsulation of the Kidneys for Eclampsia.—LONGARD (*Monatssch. f. Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 4) reports 11 cases of eclampsia treated by decapsulation of the kidneys. One died twelve days after operation, the convulsions having ceased and the secretion of urine having become established. The patient died of septic infection. She became maniacal on the third day and tore off the bandages infecting the wound. In the eleventh case the convulsions ceased after operation, and the secretion of urine increased. Death followed on the fifth day from sepsis, and autopsy showed the origin of the infection to be within the uterus. In 1 case operated upon by a colleague, but one kidney was decapsulated. Operation was performed twelve hours after delivery; death followed three hours later. It is possible that this patient's life might have been saved had both kidneys been subjected to decapsulation. In another case, in which operation was performed twelve hours after delivery, hemorrhagic nephritis, followed by complete suppression of urine, caused the patient's death. Here, evidently, operation was performed too late. A comparison of the results of this operation with the series of cases of eclampsia treated by other methods in the same hospital gives an improvement in the results with decapsulation. In the first, 55 per cent. mortality was recorded; in the second, 18.7 per cent. The clinical phenomena in these cases were practically the same. There was found in the bladder a small quantity of highly albuminous and somewhat bloody urine containing casts. After the decapsulation the quantity of urine increased and the albumin grew less, until a normal condition ensued about the fourth day. On inspection, the kidneys were a yellowish white, often with greater or smaller points of hemorrhage, the whole indicating parenchymatous nephritis. In performing the operation ether anesthesia was chosen. The operation should proceed as rapidly as possible, and double decapsulation, with suture of the wound, can be performed in from twenty to twenty-five minutes. Bergmann's incision was employed and the capsule incised the whole length of the kidney, and separated by pressure with gauze sponges down to the hilus; then the kidneys were replaced. In the first two cases the wounds were drained, but not in the remainder.

Section of the Uterus Through the Posterior Cervical Portion.—POLANO (*Zentralbl. f. Gynäk.*, 1911, No. 40) reports 4 cases of section through the uterus in the lower cervical region. In 1 case the pelvis was not contracted, but the patient, in previous pregnancies, had children very large and with very hard crania, requiring perforation. The second patient had a rachitic pelvis and was operated upon by lumbar anesthesia. Pituitrin was given hypodermically to excite

uterine contractions. The third patient had a normal pelvis, but suffered a prolonged and painful labor from premature rupture of the membranes and failure of the child to descend and engage. The fourth patient had a flat, rachitic pelvis with a true conjugate of $7\frac{1}{2}$ cm. The mothers and children in these cases did well.

The Differential Diagnosis of Ectopic Gestation.—VELITZ (*Monatssch. f. Geburts. und Gynäk.*, 1911, Band xxxiv, Heft 4) reviews his experience in 32 cases of ectopic gestation, and draws attention to the difficulties in diagnosis. The presence or absence of hematocele adds much to the difficulty of diagnosis. The practical conclusion in these cases is to consider the patient as one having a malignant growth, or, at least, a tumor requiring removal. A positive diagnosis may only be made by operation, and the conditions present dealt with in accordance with the nature of the case.

Repeated Ectopic Pregnancy.—RICHARD SMITH (*Amer. Jour. of Obstet.*, September, 1911) reports 4 cases of repeated ectopic pregnancy. In 1, upon a second operation, rupture was found with an adherent appendix and adhesions. A similar finding was present in the second case. The other 2 were typical, and all made good recoveries from the second operation. Smith has collected from American observers 1608 cases, in which 58 were subjected to a second operation. In foreign literature he finds the report of 1390 cases, in which 55 were subjected to a second operation. In his correspondence he has found 2 cases in which ectopic pregnancies occurred three times. Normal pregnancy following ectopic pregnancy occurred in his own 33 patients three times. As regards the question of treatment, he concludes that if the woman has had no children, and is young and desirous of having children, in operating for ectopic pregnancy, if the opposite tube is normal and not closed at the extremity, it should not be removed. Where the patient has had children, we should, if possible, obtain her desires upon the matter and leave the tube, unless it is absolutely closed. Where the patient has had children, and requests that both tubes be removed, this request should be carried out.

GYNECOLOGY

UNDER THE CHARGE OF

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Treatment of Injured Ureters.—STOECKEL (*Zeit. f. gyn. Urologie*, 1911, iii, 51) calls attention to the fact that while obstetric injury to the ureters is becoming less frequent, owing to earlier interference in difficult cases, gynecological injuries are increasing greatly in frequency, because of the increase of extensive operations—especially the radical

operation for carcinoma of the uterus—and also due to the fact that many inexperienced operators are now attempting these difficult operations. Stoeckel asserts most emphatically that in all cases, except where a malignant growth is present, it is the fault of the operator if the ureter is injured. It matters not in these cases whether the ureters follow a normal course or are displaced by a tumor, or whether the operation is performed by the abdominal or vaginal route, injury to the ureter is always avoidable if proper precautions are taken. Where a malignant growth is present, however, it is a different story. Here it may be necessary to isolate the ureter for long distances, to dig it out from its carcinomatous bed, to cut through it, or to resect it. The author has found that the ureter can stand simple isolation from the surrounding tissue for a distance of 10 cm. or more without undergoing necrosis. Such ureters may later become compressed by contracting scar tissue around them, but they never become obliterated, or even dangerously stenosed, except by recurrence of a malignant growth. The ureter that must be dug out of an indurated, carcinomatous bed always presents the possibility, however, of becoming secondarily infected, owing to the injury to its walls, this leading to pyelonephritis or to secondary fistula formation. It may also become the seat of a recurrence of the neoplasm, this occurring, Stoeckel believes, much less infrequently than has been assumed. In very bad cases he recommends, therefore, resection of the ureter on the worst side; he does not favor bilateral resection, as bilateral implantation into the bladder is much more difficult and less certain of success than unilateral. While many ureteral fistulæ heal spontaneously, this is often accompanied by a total or partial occlusion of the ureter, with corresponding reduction or elimination of the function of that kidney; moreover, long waiting for a fistula to heal favors ascending infection. The principle of waiting for months should, therefore, be given up in favor of operation within a few weeks at most. The proper method of treatment is resection and implantation of the ureter into the bladder by the abdominal route, if this is possible. Direct closure of a ureteral fistula by suture of the walls should be limited to cases in which the injury involves less than one-third of the circumference of the ureter, as otherwise stenosis is apt to occur. In doing the implantation the fundus of the bladder should be brought well over to the affected side, so as to cause less tension on the sutures. It is important not simply to make a slit in the bladder wall, but to cut out a little circular piece of tissue, as the opening made in the latter way is much less likely to undergo subsequent contraction. To still further prevent this, the bladder mucosa is stitched to the serosa around the entire edge of the opening, so as to prevent the formation of a granulating wound. The ureter is then passed through this opening so that it projects well into the bladder, and is held in place by fine *absorbable* sutures to the bladder wall, the latter being folded back along the ureter for a considerable distance. Stoeckel demands that the merits of all operations for restoring the function of the injured ureter be judged by the lasting physiological results, these being ascertained by cystoscopic examination at least three years after operation. Where pyelitis or pyelonephrosis is already present, of course a nephrectomy should be done at once. Implantation of the ureters into the intestinal tract or onto

the skin surface should be given up, as both these methods lead eventually to infection and nephrectomy. A simple and oftentimes very useful method of treatment where implantation is impossible, owing to the length of the resected portion, is the ligation of the end of the ureter, with consequent elimination of the corresponding kidney. To accomplish this the ureter should be kinked on itself once or twice, as simple ligation may give way.

Direct Suture of Severed Ureter.—FORSSELL (*Zentralbl. f. Chir.*, 1911, xxxviii, 1369) expresses views somewhat different from those of Stoeckel, and describes the following method, by which he repaired by direct end-to-end anastomosis a ureter which he had accidentally severed. The wall of the vesical stump of the ureter was slit longitudinally for a distance of 1 cm. from its transversely severed end. Its mucosa was then removed for a distance of 0.5 cm. from the severed end, this being accomplished without difficulty after securing fixation of the end of the ureter. The end of the renal portion of the ureter was then drawn *into* the vesical portion by means of a mattress suture of catgut, which passed through all coats of both stumps a couple of millimeters from the free edge of the mucosa. This was placed on the side directly opposite to the longitudinal slit in the vesical stump, and was knotted on the outside of this. The longitudinal slit was then closed by a couple of interrupted catgut sutures, and the transversely cut edge of the lower stump was fastened in a similar manner to the outer surface of the upper. There was no leakage. Cystoscopic examination nearly two years later showed urine being rhythmically expelled from this ureter, and the ureteral catheter passed the point of injury without any evidence of obstruction. Forssell thinks that this method, where it can be carried out, is preferable to vesical implantation, because it is simple, causes no secondary stricture, leaves the vesical orifice of the ureter intact, and does not sacrifice any considerable length of the ureter.

Treatment of Vaginismus.—FUNK-BRENTANO (*La Gynécologie*, 1911, xv, 633) reports having treated most successfully three cases of vaginismus in recently married women by the following method. Under chloroform anesthesia a Champetier de Ribes bag having a diameter of 5 to 6 cm. is introduced into the vagina, and is then slowly and gradually dilated. It must be remembered in doing this that the extensibility of the parts is much less than in pregnant women, and care should be taken to avoid tears of the vaginal walls. When the bag is full it is pulled upon, so that the perineum bulges and the bag protrudes through the orifice. The hymen is thus put on the stretch, and can be very easily excised. Having done this completely, several little incisions 1 to 2 mm. deep are made around the ring where the base of the hymen was attached. The bag is then extracted without using violence, and a larger one, having a diameter of 7 to 8 cm., is introduced and inflated in the same manner. Great care must be taken in extracting this bag, as much time being employed as in delivering the head in labor. The vaginal orifice now presents the appearance as if labor had just been completed. A manual examination should be made to see if there are any tears, and if such are found they must be

sutured. The procedure is concluded by tamponing the vagina with gauze, which is removed the next day. After this injections are made twice daily into the vagina by means of a well greased, smooth, metal, cannula, the size of which is gradually increased, without the patient being aware of this. Funk-Brentano believes that this method is much superior to the use of specula, as all the muscles of the pelvic floor, especially the levator ani, are stretched by the bags.

Small Fibroids as Cause of Dysmenorrhea.—WILSON (*Brit. Med. Jour.*, 1911, No. 2651, p. 996) relates 3 cases of dysmenorrhea in single women, aged about thirty-two years, in which he thinks the presence of small fibroids was the causative factor. In 2 of the cases the uterus was removed; in 1 of these uteri a small interstitial fibroid, about 7 mm. in diameter, was found in the isthmus; in the other, two similar small nodules were found in the same situation. In the third case a vaginal celiotomy was performed, and the presence of an interstitial fibroid about the size of a hazel nut at the level of the isthmus recognized. This was removed by simple enucleation. All the cases were cured of their symptoms. Wilson believes that the menstruating uterus exhibits a certain degree of "polarity," i. e., the body undergoes intermittent contractions, the cervix dilating at the same time. Anything which interferes with these functions, especially the regular and easy dilatation of the internal os, may be expected to cause pain, and nothing is more likely than that a fibroid of even small size situated in the wall at the level of the isthmus may give rise to such interference.

Vaccine Treatment of Pelvic and Allied Infections.—For the past two years POLAK (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1738) has used vaccine therapy in almost every case of septic infection occurring in his obstetrical and gynecological services, irrespective of the time at which it was first seen, his experience for this period covering about 225 cases of various sorts of pelvic and allied infections. He considers the phagocytes the chief factors in combating streptococcic, staphylococcic, and gonococcic infections; these are distinctly increased by bacterial vaccines when used early enough. The prognosis is best when the process is local; where a violent bacteremia has existed for some time vaccines accomplish little. Polak has found that autogenous vaccines from a single strain give unreliable results, and are much inferior to mixed, polyvalent vaccines from reliable laboratories. Following an injection of these the leukocyte count is usually increased and the polynuclear percentage decreased. It is best to start with a relatively small dose, 25,000,000 to 100,000,000 in most cases, counting the blood four hours before and eight hours after the injection, subsequent dosage being regulated according to the effect produced on the leukocyte count by the initial injection. As a result of his experience, Polak concludes that vaccines are of positive value in thrombophlebitis, and in colon bacillus or mixed pyelitis; in 2 cases of suppurative mastitis they also appeared to be of great service. In the various other forms of infection in which he has used them their value has been more or less uncertain, though in many cases they appear to have aided nature in effecting a cure.

OPHTHALMOLOGY

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New Hypothesis of the Pathogenesis of Nystagmus.—None of the hypotheses thus far advanced to explain the production of nystagmus is entirely satisfactory. Arlt's view that the subjects affected with nystagmus displace their eyes in order to supplement a lack of clearness of the image by an additional number of such images in series cannot apply to those numerous cases in which the vision is greatly lowered, but which do not become nystagmic, while others become so with normal or almost normal visual acuity. On the other hand, many children with congenital blindness show typical nystagmus. Moreover, it would be a mistake to believe that ocular disturbances are alone capable of producing nystagmus. The latter has been frequently observed after otitic suppuration. SAUVINEAU (*Annal. d'Oculist.*, April, 1910, p. 295) holds that nystagmus is due to disturbances or lesions affecting the supranuclear centre which presides over the lateral associated movements, as proved by the fact that when recent it is *habitually* accompanied by a latent diplopia, of which the subject is himself ignorant, but which can be brought out by careful testing with a red glass. Ocular lesions determine the nystagmus when favored by fault of development of the innervation centres of lateral associated movements. This explains why the same ocular lesion does not cause nystagmus in all who are affected with that lesion.

Idiopathic Ciliary Neuralgia.—MONCORGÉ (*La Clin. Ophtal.*, May, 1911, p. 190) calls attention to a form of severe pain, generally unilateral, in and about the eye without any objective symptoms; the pain is usually diurnal, increases on palpation, and occurs more frequently in men than in women. The affection seems to be entirely independent of the refraction; it has been found to occur in eyes entirely normal. Moncorgé is disposed to believe that this functional affection is a principal if not the sole cause of the ordinary headache of undefined character.

Amblyopia Exanopsia.—From an exhaustive study of the pathogenesis of amblyopia exanopsia and strabismus, CAILLAUD (*Annal. d'Oculist.*, December, 1910, p. 385) concludes that there exists an amblyopia from non-use; amblyopia without objective lesion is most frequently congenital, though it may be acquired; the age is without influence upon the degrees of impairment; it is found in hypermetropia, myopia, or astigmatism. A nisometropia appears to have great influence upon the production and degree of the amblyopia, high degrees of which

often accompany slight differences in the refraction of the two eyes. Where such differences are great (3 to 8 D), there is usually but little amblyopia. Weakness of the accommodation does not appear to be a factor. *The amblyopia precedes the strabismus; the latter has no influence upon the development of the amblyopia.* The strabismus only becomes fixed in one eye when the visual acuity of the latter is inferior to its congener; if the visual acuity is equal in the two eyes the strabismus will be the alternating variety.

Exophthalmic Goitre.—FEDERN (*Wien. klin. Woch.*, 1910, No. 16, p. 298) maintains that the disease is due to abnormally high blood pressure. Such elevation depends, as a rule, upon disturbance of the functions of the intestines, which disturbance Federn ascribes to partial atony of the bowel. The disease may also occur as a consequence of other disturbances which result in elevation of the blood pressure. Such disturbances may be seated in the genital system, or may be due to worry, mental overexertion, etc., all conditions which generally cause intestinal disturbances. In many cases an acute element also enters which seems to bring about a sudden development of the affection, but which is really to be regarded as simply an aggravation of an already present, but latent, condition, plus the development of additional symptoms.

Intoxication by Atropine in Children.—COLIN (*La Clin. Ophthalmol.*, December 10, 1910, p. 589) has frequently observed evanescent erythema of the face, chest, and abdomen follow instillations of 0.5 to 1 per cent. aqueous solution of atropine in children aged between two and seven years. Prostration or delirium, so frequently noted in adults, was never observed. In some children the erythema regularly followed each instillation. Most of the subjects were affected with phlyctenular ophthalmia, arguing a reduced condition of the system. The phenomena were particularly noted during the inflammatory attacks, much less frequently in intervals of quiescence. These accidents became very infrequent when collyria in oil were substituted for the aqueous; if the latter are employed the lacrymal puncta should be compressed with the finger.

The Behavior of the Ciliary Body to Antibodies.—SALUS (*Graefe's Archiv*, lxxv, 1) shows that complement cannot be demonstrated in normal aqueous humor. Different antibodies do not pass in the same way into the normal aqueous. Agglutinins and antitoxins pass easiest, while the migration of bacteriolysins is more difficult, and hemolysins the most difficult. The aqueous formed immediately after paracentesis is rich in antibodies, although not to the same extent as serum. The normal ciliary body is completely impervious to albuminous precipitates, but after paracentesis, such precipitates appear in the aqueous; they even appear to occur there with special rapidity. The absolute retention of the precipitates can hardly depend upon special properties of the same; it must be assumed that a certain filtration faculty is possessed by the transuding organ—the capillary endothelium or epithelium of the ciliary body. If the experiment is properly arranged, the precipitation can be followed in the anterior chamber as in a

test-tube. When paracentesis is practised upon an animal which has been treated with human serum, the newly formed aqueous shows distinct flocculent cloudiness. Hemolysins can likewise be shown by the red stain of the aqueous humor. This phenomenon comes out with special distinctness after paracentesis of the anterior chamber.

Ophthalmic Notes in Madagascar.—CRENN, Surgeon-Major in the French Colonial Army (*La Clin. Ophthalmol.*, October 10, 1910, p. 547), from an experience of ten years in medical posts in Madagascar, finds that although that country is affected with paludism in its most severe forms, the ocular affections of malaria are very rare. The lesions observed seem to depend upon the resulting anemia or toxemia. Trachoma is not present, and glaucoma extremely rare; he has only observed a single case. The natives are all hyperopes or emmetropes. Myopia was not found except in a few young school children. He never observed detachment of the retina. The ocular manifestations of acquired syphilis are less grave than in Europe, due, no doubt, to the absence of alcohol, tobacco, and perhaps, myopia.

Treatment of Incipient Senile Cataract with Instillations of Salts of Iodine into the Eye.—KATZ (*Klin. ther. Woch.*, 1910, pp. 36 and 37), in the course of eleven years, has treated more than 60 cases of incipient senile cataract with instillations of sodium iodide. He begins with a 5 per cent. solution, which is progressively reduced to 1 per cent. if the slightest irritation of the conjunctiva occurs. The collyrium was employed at bedtime and from one-half to one hour before rising in the morning. The influence of the instillations upon the course of the opacity is asserted to be marked. In a decided series of cases the treatment inhibited the development of the cataract with the consequent decrease of the visual acuity, or even caused a clearing up to a certain extent of opacities already present.

Retinal Hemorrhage.—ROGERS (*Jour. Amer. Med. Assoc.*, July 8, 1911, p. 99) has made a study of this condition based upon 187 personal cases, omitting specific retinitis, he has classified them as retinal apoplexy, and under five varieties of retinitis, namely, simple hemorrhagic, albuminuric, diabetic, and chorioretinitis. His conclusions are that three-quarters of all cases of hemorrhagic retinitis either terminate fatally within a few years or the subjects suffer marked impairment of health. The prognosis as to life in albuminuric retinitis is better as the patient is older. Any form of hemorrhagic retinitis is suggestive of either present or future disease of either the nervous or circulatory system.

Subhyaloid and Vitreous Hemorrhages.—WOODS (*Jour. Amer. Med. Assoc.*, July 29, 1911, p. 375) concludes that in persons, aged over fifty years, with such hemorrhages, the sign of arteriosclerosis are usually present, or, if not, the hemorrhage itself is evidencce. In young subjects there is probably some infection or disease capable of producing vascular changes. When no cause can be found it is nevertheless usually of a serious nature, such as tuberculosis, nephritis, or defective metabolism.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Frambesia, Syphilis, and Salvarsan.—RICHARD D. STRONG communicated to the *Journal of Experimental Medicine* (April 1, 1911) a statement of the great success he has met with in 25 cases of yaws, treated by salvarsan. The usual adult dose, given in the usual way, has produced in yaws the results which we are accustomed to see in syphilis, and has produced them with the same degree of promptitude. It will be remembered that public opinion, which of late rather inclined to the view that yaws and syphilis were identical, has now once more come to consider them as different. Yaws is thought to be due to the *treponema pertenuis*, and the inoculation of both diseases into monkeys is very suggestive as indicating their disparity. It will be remembered by everyone who has been interested in the subject that no previous treatment of yaws has been in any sense satisfactory.

Distemper in Dogs.—Although, fortunately, distemper of dogs is not communicable to the human race, yet the disease is widely known and of such household interest that it is interesting to see that FERRY (*Journal of Infectious Diseases*, June 15, 1911, vol. viii, No. 4) has been able to verify his statement made last year that the disease is due to the bacillus which he then named *bronchicanis*. His observations indicate that early in the disease *Bacillus bronchicanis* can be isolated in pure culture in all cases. If the investigator waits until the discharge from the respiratory tract makes its appearance, the cultivation of the organism is much more difficult by reason of the secondary organisms which are present. In a fair percentage of cases it was found in the blood, and Ferry was unable to isolate it during life, in the very earliest stages of the disease by use of the bronchoscope. Artificial inoculation with pure cultures has produced the typical disease, and from these cases again the organism has been isolated in pure culture. Further, the serum of dogs suffering with distemper gives positive agglutination with the organism, while the controls have been constantly negative. Ferry is to be congratulated upon a well-rounded and convincing piece of work.

Experimental Typhoid Fever.—METCHNIKOFF and BESREDKA (*Annales de l'Institut Pasteur*, March, 1911) detailed the experiments by which they have successfully inoculated anthropoid apes with the bacillus of Eberth. Considering the difficulties that have previously surrounded experimentation in the lower animals, they were led to ask themselves if the bacillus typhosus was the real cause of the dis-

ease, or whether, as in the case of the bacillus of hog cholera, the scientific world had not been considering the secondary organism as primary and overlooking some minute organism which might prove to be the real cause. Instead of using pure cultures, they began with feces from a typhoid patient, with the result that the young chimpanzee used developed a satisfactory attack of typhoid fever. Further, the fecal typhoid material was filtered, the filtrate given by the intestinal tract, and the rest injected under the skin. This was repeatedly unsuccessful. Not only was it impossible to infect in this way, but it was impossible to protect. Fifteen experiments out of sixteen, using pure cultures of human typhoid or mixed cultures of human and simian typhoid, were successful. The blood of the infected animals in every case developed rapidly agglutinative powers. Experimental typhoid in chimpanzees bears to the ordinary typhoid fever of adults much the same relation as does that of children. There is less prostration, less weakness, less anorexia and apparently no rose spots. The older the ape the more his disease resembles that with which we are familiar. In the three fatal cases that occurred in the series, autopsy showed marked enterocolitis, with great swelling of the Peyer's patches, but never ulceration. Numerous attempts with the infected material of the higher apes proved negative in the production of the disease in monkeys and in other laboratory animals. Metchnikoff and Besredka conclude that experimental typhoid in animals can be produced only in the higher apes and only by way of the intestinal tract. Their positive results were obtained by pure culture of the bacillus of Eberth, and they conclude that there exists no soluble virus to play a subsidiary or primary role in the infection. Vaccination which has proved sufficient to protect laboratory animals against peritoneal infection by *Bacillus typhosus* is powerless to prevent the typhoid fever of apes, which appears to be the real disease with which we are familiar.

Bone Lesions in Infective Diseases.—JOSEF KOCH (*Zeit. f. Hyg. u. Infekt.*, Band lxxix, Heft, 3, 1911), who has been a strong advocate of the infective nature of rickets, brings forward further experimental work in support of that contention. In various kinds of experimental animals he has examined the localization of the injected bacteria in the bony structures. In 20 anthrax-infected animals great, sometimes enormous, masses of bacilli were found in the epiphyseal marrow, especially in the primary medullary spaces of the line of ossification, notably in close association with the vascular loops. Pneumococci appeared to frequent, in addition, the areas of endochondral ossification, and streptococci the perichondrium and periosteum. The great destruction of bacteria that goes on in the medulla is evidenced by the pigment seen in the endothelial cells, and the bacteria found at death constitute only a fraction of the bacteria that have existed there during the course of the infection. The histological changes which are evident as a result of the infection are very marked, both in compact and spongy bone. The spongy bone may be destroyed and the absorption of compact bone greatly hastened. In the general infections, although the heart blood may prove sterile, the juice of the epiphyseal medulla is by no means so, and frequently shows the presence of bacteria. Even in the acute infections of children, such as measles and whooping cough,

the same thing is noted, thanks partly to the osteochondral boundaries in children being a site of predilection for infection. It is true that the pathogenic bacteria, after a time of increase, may be destroyed by specific antibodies, but this short time may be long enough to institute changes in the epiphyses; and the histological changes seen in rachitic bones are oftentimes of a regenerative kind. In 2 cases of florid rickets, with a fatal outcome, Koeh found in the femoral epiphyses large numbers of bacteria, and he thinks that the cause of rickets is not to be sought in indefinite *noxæ*, but in bacteria.

Co-incident Abnormality of Numerous Organs of Internal Secretion.—F. HARBITZ (*Zentralbl. f. Allg. Path. u. Path. Anat.*, Band xxii, No. 18, September 30, 1911) reports a case that is very suggestive in its bearing upon the relation that exists among the glands of internal secretion. Autopsy was performed upon a man, aged forty-three years, who had acromegaly which had evidently arisen from hyperplasia of the hypophysis. There was seen hyperplasia of the tissues of the hands, feet, and face, and of many internal organs, especially of the right side of the tongue, larynx, and trachea, of the hypophysis, liver, spleen, right kidney, heart, thyroid, and pancreas—in short, splanchnomegaly. Further, there was hemiatrophy of the left side of the face, of the larynx, and of the trachea, which Harbitz does not feel competent to explain; but in the absence of a discoverable lesion of the trigeminal nerve, of any muscular lesion, and of syringomyelia, he believes that these atrophies must depend upon a lack in the *anlagen* of the organs concerned, especially since the left kidney was similarly affected. More than a coincidence is the fact that not only the hypophysis and the thyroid were enlarged, but the pancreas and other organs of internal secretion. Harbitz recalls the effect of the hypophyseal secretion on structural growth in general, and the repression of acromegaly after removal of tumors of the organ, as evidenced by Hoehenegg, Cushing, etc., as well as the linking that seems to exist between the hypophysis and thyroid on the one hand, and obesity and the failure in genital functions on the other, or again the concurrence of the two last, which Frölich united in the title of *dystrophia adiposa genitalis*. Damage to the glial portion of the hypophysis appears to cause these genital hypoplasias. Harbitz seems to have brought forward another of these interesting cases that appear to show that the glands of internal secretion are intimately associated, and that there is a "polyglandular syndrome," often caused by "pluriglandular insufficiency," but sometimes by what appears to be rather "oversufficiency" of the same structures. Some interesting certainties are arising in this field of unproved suppositions.

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DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

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THE
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ORIGINAL ARTICLES

CECUM MOBILE.¹

By JOSEPH SAILER, M.D.,

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By cecum mobile is meant an abnormal motility of the cecum and lower portion of the ascending colon. This may be purely anatomical and give rise to no clinical symptoms, or, as a result of movement of the cecum, kinks may be produced, causing partial or temporary obstruction ultimately giving rise to more or less atony and dilatation of the cecum with associated clinical symptoms.

The term was first employed by Haussmann,² who in 1904 reported 8 cases characterized by fairly similar clinical signs, the cause of which he ascribed to this abnormal condition whose existence he determined purely by physical examination.

The various malpositions of the large bowel have been the subject of attention on the part of anatomists for many centuries, and Schultz³ has collected the description of these anomalies in Morgagni's writings. Curschmann,⁴ in 1894, was the first to attempt a systematic study of the possible relation of these malpositions to various clinical manifestations. In the course of this article he describes several cases of reflection upward of the cecum with a

¹ Read before the College of Physicians of Philadelphia, November 1, 1911.

² Berlin. klin. Woch., 1904, No. 44, p. 1153.

³ Case 14. "The beginning of the ascending colon lay deeper than normal." Case 19. "The ascending colon was so bent and doubled upon itself that the fundus of the cecum, directed upward, touched the portion of the transverse colon lying under the liver." Case 3. "The colon overlying the small intestines passed upward from the right hypochondrium to the umbilicus." Vesalius has pictured the reflection upward of the colon.

⁴ Deutsch. Archiv f. klin. Med., 1894, liii, 1.

sharp kink that caused complete obstruction; in one instance the blind end of the cecum was close to the edge of the liver. He was able to demonstrate that anomalies of the mesentery and mesocolon were responsible for these displacements, and therefore indirectly for the clinical symptoms. He noted also that when the attachment of the mesocolon of the cecum to the posterior parietal peritoneum did not occur, the cecum might be found in the region of the umbilicus, giving rise to a "Wander cecum" or floating cecum.

Hausmann's 8 cases were all characterized by attacks of colic, usually beginning with constipation, and the presence during the attacks of a movable tumor in the right lower quadrant of the abdomen that could be pushed upward leaving an empty space in the right iliac fossa. The number of his cases has since been increased to 143, none of which, curiously enough, at the time of his last publication, had been confirmed either by autopsy or operation, chiefly he complains because consultants did not recognize the existence of the condition, and therefore would not concur in the diagnosis. His paper attracted very little attention, and it was not until Wilms⁵ reported 40 operative cases that the physicians of Germany began to regard cecum mobile as an actual clinical disease. He had observed that many cases of so-called chronic appendicitis were not relieved by appendectomy, particularly if the appendix was not adherent, and inferred that his inability to obtain statistics regarding the end results of operations for chronic appendicitis was due to the uncertainty and indefinite character of the benefit derived from them. It occurred to him, therefore, that other factors than disease of the appendix might be active in causing the symptoms, and after some study he reached the conclusion that the pain at least might be due to a long cecum mobile. This might permit the stretching or tearing of the nerves in the mesentery and mesenterium, and at any rate be responsible for the tenderness at McBurney's point. These cases in which the appendix and cecum are freely movable, are theoretically not curable by appendectomy alone, and accordingly he devised an operation for the fixation of the cecum by means of broad adhesions to a sort of pocket formed in the iliac fossa. In 40 cases this gave good results.

The observation of Wilms that operations in cases of so-called chronic appendicitis failed in many cases to relieve the symptoms had been frequently made by clinicians prior to the publication of his article. Albu,⁶ in particular, had called attention to this point, although he did not suggest any satisfactory explanation. It is noteworthy that in the text-books of neither Deaver nor Kelly are any statistical studies made of their operative results in these conditions, although the experience of both must be very large.

⁵ Deut. med. Woch., 1908, p. 1756; Zentralbl. f. Chirurgie, September 12, 1908, p. 217.

⁶ Deutsch. med. Woch., 1905, No. 26, p. 1065.

In the brief period that has elapsed since Wilms' article, cecum mobile has excited the liveliest interest among the German and Russian internists and surgeons. Fischler,⁷ in 1909, was able to report 41 cases and to give the first comprehensive description of the symptoms from the medical standpoint, and Klose,⁸ in a series of articles published in 1910, again discussed the diagnosis and reported the results of surgical measures in 12 cases. Of these 12 the first 7 were discovered only after the abdomen had been opened, but with the experience gained from these the last 5 were diagnosed before operation. Wiemann,⁹ Heiler,¹⁰ and Straschenko,¹¹ have also reported cases and discussed the condition. So far as I know, it has not attracted the attention of French, English, or American medical writers.

The anatomical basis appears to be a congenital malformation of the mesocolon of the cecum, of such a nature that for some distance along the ascending colon it maintains the type of the mesentery and is not attached to the parietal peritoneum.¹² This permits to the part at large all the freedom of movement characteristic of a loop of small intestines, and, indeed, as a result of the greater length of the mesentery and the less confined position of the first portion of the colon, considerably greater displacement may take place. That this malformation occurs, as the Germans contend, in the latter part of the second month of pregnancy appears to me to be an illogical assumption. It first becomes manifest when the primitive gut begins to differentiate, but the predisposition must exist from the beginning of independent embryonal existence. This defect of the mesocolon is, of course, not in itself a morbid condition, and may exist without giving rise to any clinical manifestations whatever, but it renders certain forms of obstruction possible that cause the attacks and secondarily the distention and atony of the cecum. These obstructions are of three types: (1) The formation of a kink usually near and below the hepatic flexure; (2) the reflection upward and forward of the cecum upon the ascending colon until, indeed, in the most extreme cases, the caput coli may touch the liver; (3) volvulus of the cecum. Two cases of the second type and one of the third type were reported by Curschmann. These, however, are not the only lesions that may give rise to these symptoms, for not less than 3 of Klose's 12 cases showed at operation, adhesions pulling the cecum downward and thus producing obstruction.

⁷ Mitteil. a. d. Grenzgebiet d. Med. u. Chir., 1909, xx, 663.

⁸ Beiträge z. klin. Chirurgie, 1909, vol. lxxiii, Heft 3; Fortschr. d. Med., 1909, No. 16; Münch. med. Woch., 1910, p. 348.

⁹ Deutsche med. Woch., 1909, p. 146.

¹⁰ Münch. med. Woch., 1910, No. 11, p. 587.

¹¹ Archiv. f. Verdauungskrankheiten, Band xvii, Heft 1.

¹² This condition usually extends for from one-half to two-thirds of the length of the ascending colon, according to Wandel, and in six of his seven cases as far as the liver.

Haussmann recognizes two varieties—(1) passive mobility, and (2) spontaneous mobility. The latter is subdivided into three types according to the level to which the caput coli can be displaced—to the crest of the ilium, above the crest, and to the costal margin. I have yet to observe a case in which I could demonstrate to my satisfaction any such extreme motility as in the third type.

There appears to be much difference of opinion regarding its frequency, a difference due in large part to varying standards. It is, therefore, impossible to compare or even to attempt to reconcile the figures that have been given by various investigators. Thus an abnormally movable cecum was found by Engel,¹³ in 10 per cent. of the subjects he examined; Treves¹⁴ found extreme motility in 11 of his 100 dissections; Dreicka found a common mesentery of the ileum and cecum in 23 per cent. of the cadavers that he examined. The most important statistics are those given by Wandel.¹⁵ In 640 autopsies carefully studied with reference to this particular point, he found in 66 mobility of sufficient degree to permit kinking, torsion or displacement; of these, 28 were children, and although the whole number of children examined is not given, it is stated that the proportion is greater than in adults. In 8 of the 66 cases, the cecum was turned forward and upward, but in the majority the position of the organ was normal. In regard to the frequency with which symptoms are produced, I have found only one definite statement. During the period in which Klose and Rehn operated upon 12 cases of cecum mobile, they also operated upon 80 cases of chronic appendicitis; that is, 15 per cent. of all supposed cases of chronic appendicitis may be due to cecum mobile.

The figures of Haussmann¹⁶—143 cases observed in six years—indicate an enormous clinical material; a readiness to make the diagnosis, or a singular blindness on the part of the whole medical profession to a very common condition. Fischler gives no definite figures, but is content to surmise that “a large part of the troubles heretofore collected under the name of chronic appendicitis is due to a more or less pronounced muscular insufficiency of the cecum, a typhlatonia.” He has observed 41 cases, but fails to state in how long a period, or what proportion they formed of his other cases. Indirect evidence may be found in the article of Wandel, who has collected from the literature a large number of cases of volvulus of the cecum and ascending colon which were only possible as a result of their abnormal mobility.

There appears to be some difference of opinion regarding the symptomatology of these cases. According to Fischler the clinical

¹³ Wien. med. Woch., 1857, No. 30 to 41, p. 553 et seq.

¹⁴ British Medical Journal, 1885, p. 474.

¹⁵ Mitteil. a. d. Grenzgebiete d. Medizin u. d. Chirurgie, vol. xi, p. 39.

¹⁶ Die methodische Intestinale Palpation, Berlin, 1910.

picture is fairly uniform. Attacks of colic occur at irregular intervals, but with a general tendency to increase in frequency, severity, and duration. Each usually begins with a longer or shorter period of constipation, and there is severe pain lasting for a few hours, about two according to Klose, or more rarely for several days, and terminating in a copious discharge of feces. During the attack there is loss of appetite and perhaps nausea and even vomiting; the temperature is either normal or, if fever occurs, it is slight. The leukocyte count is normal. A mass can be felt in the right lower quadrant about the size of a small apple, firm, but not hard, and elastic, but not doughy. Nothing can be felt on the left side. Tenderness is usually present, and is most distinct near McBurney's point. Gurgling can usually be elicited. Posture has a pronounced effect upon the pain. If the patient stands or sits the pain is worse. It is relieved, and indeed the attack may sometimes be terminated, if the patient lies upon the back or particularly upon the right side. Predisposing factors are exertion and the indulgence in food that produces flatulence. During the interval the patient may be subjectively well, but usually symptoms of chronic colitis are present; that is, alternating diarrhea and constipation, mucus in the stools, and intestinal flatus. In spite of Fischler's large experience, it seems that such a characteristic clinical picture cannot be present in the majority of cases, and I am, therefore, more inclined to agree with Wiemann,¹⁷ who believes that obstinate constipation not yielding to laxatives is the most characteristic feature. Haussmann is more interested in the physical examination of his patients than in the symptomatology. Klose apparently considers that the symptom complex ascribed to chronic appendicitis is also the symptom complex of cecum mobile.

The physical signs are those by which the displacement, the distention, and the atony of the cecum are recognized. They may be divided into signs obtained by palpation, by inflation of the colon, and by the x-rays. That the cecum can be palpated in a large percentage of cases is no longer a matter of dispute. Clinicians have obtained somewhat different figures, depending upon their skill and material, since Franz Glenard first described the *boudin cecale*. Obrastow,¹⁸ in 109 men found a palpable cecum 56 times, or in 51.4 per cent., and in 60 women, 35 times, or 58 per cent. Haussmann claims to have palpated the cecum in no less than 256 of 300 persons, or in 80 per cent.

In order to test this subject I have analyzed the results of the physical examinations of the abdomen made upon 312 office patients within the last year. The conditions of the examinations in all these patients were approximately the same. They were all

¹⁷ Deut. med. Woch., 1909, p. 146.

¹⁸ Archiv f. Verdauungskrankheiten, vol. i, p. 265.

ambulant patients, and represented a considerable variety of clinical conditions, many of them having no symptoms referable to the abdomen whatever. Sixty-two, or about 20 per cent. had a distinctly palpable cecum. This varied from a soft, indefinite, movable mass to a distinctly palpable, tympanitic, balloon-like body. The position was variable, in some cases nearer the anterior superior spine, and in others nearer the median line. The lower edge, as determined by palpation and percussion, varied between a point 2 inches below the interspinal line to a point 1 inch above it. In many cases no note was made of its exact position, and therefore the frequency of these variations cannot be given. In nineteen of these sixty-two cases, that is, in about 30 per cent., there was more or less tenderness. As a rule, this amounted merely to some discomfort upon deep firm pressure, and was not associated with flinching or rigidity. Tenderness of this character was not recorded as such unless it was not present simultaneously at the corresponding point on the left side. In a few cases there was slight rigidity. There were no cases of certain acute appendicitis seen in the office. In 52 cases, about 17 per cent., there was slight tenderness of about the same degree over McBurney's point, not associated with a palpable colon. This was frequently variable, being found only once in a series of observations. At other times it was more or less constant, and probably indicated the existence of a chronic appendicitis or of some other inflammatory lesion in this region.

In the atonic condition the cecum is felt as a somewhat indistinct cylindrical or pear-shaped mass that can be passively displaced. It is usually tender, but rigidity and flinching are rarely observed. If present they suggest an inflammatory complication. Gurgling on pressure is a characteristic sign, splashing is rare. It may be possible to cause air to pass through the ileocecal valve into the ileum according to Hertz's method, but this would be at best difficult to recognize. A diminished resistance just below McBurney's point, or a hollowness of the iliac fossa due to the upward movement of the cecum has also been noted by Haussmann. Inflation gives rise to two signs—disproportionate distention of the cecum and more or less evidence of insufficiency of the ileocecal valve. Regarding the former the explanation of Anschuetz¹⁹ appears to have been unreservedly accepted. This is as follows: If two dilatable bodies with walls of the same elasticity are subjected to the same dilating force, the degree of dilatation is proportionate to the squares of the diameters. That is, if the lumen of the cecum is two or three times as great as that of the transverse or descending colon, the former will be dilated from four to nine times as much. Evidence of insufficiency of the ileocecal valve is the tympanitic distention

¹⁹ Archiv f. klin. Chirurgie, 1902, lxxviii, 195.

of the central parts of the abdomen. This condition was carefully studied by Hertz,²⁰ who ascribed to it the symptoms of constipation and flatulence. He also observed, in 1902, cases that might now be diagnosticated as typhlatonia or cecum mobile. The experimental inflation of the colon in these cases nearly always precipitates a characteristic attack.

The information yielded by the x -ray pictures of the colon has been studied carefully only by Klose. Ordinarily at the end of twenty-four hours a suspension of bismuth taken by the mouth is found in the descending colon and the rectum. In cecum mobile it remains in the cecum for two or three days. This finding, however, is only significant if associated with other clinical manifestations of the condition, and, if absent, cecum mobile cannot always be excluded, for at the end of an attack the bismuth rapidly disappears from the cecum. I am inclined to believe that this will also be found to be true during the normal intervals. Straschenko believes that the x -rays are of little aid in the diagnosis.

I have had x -rays taken of 5 cases in which I suspected cecum mobile, for the purpose of determining whether bismuth persisted in the cecum for more than forty-eight hours. Four cases were positive and 1 negative. In all the positive cases the persistence of the bismuth in other portions of the colon, especially the transverse and descending colon, was quite as marked as it was in the cecum, although, as can be seen from the illustrations, the cecum appears to be a region of particular accumulation, and there is a somewhat clearer area in the neighborhood of the hepatic flexure. This accumulation in the transverse and descending colon, is not noted by Klose, perhaps, because he considers it comparatively unimportant or because it did not occur. It is in my experience, and in the experience of Dr. Pancoast and Dr. Pfahler, not uncommon. It seems to me that it suggests that possibly more factors than the mobility of the cecum and lower part of the ascending colon are involved in these cases.

The clinical picture is still, as Wiemann says, uncertain. The differential diagnosis is as yet based rather upon theoretical than upon practical considerations. Cecum mobile is commonly mistaken for chronic appendicitis, and the distinction is rendered more difficult by the probability that the appendicitis forms a frequent complication. As Klose and Rehn, and Wilms, the only surgeons to report any number of cases, invariably remove the appendix, its role in the production of the symptoms can only be guessed. Wilms, however, in 5 cases removed the appendix and did not fix the colon, and none of them were benefited by the partial operation. For the direct diagnosis, Wilms depends upon the possibility of bringing the cecum to a position in front of the wound; Klose,

²⁰ Wien. klin. Woch., 1902, p. 347.

upon the retention of the bismuth in the cecum for more than forty-eight hours. Tenderness over McBurney's point and constipation are common symptoms; the signs of distended or relaxed colon, the gurgling on palpation, and particularly the attacks of pain relieved by posture, when it can be obtained, may suggest abnormal mobility of the cecum or typhltonia. Of the other confusing conditions, the most important are probably disease of the right ovary or tube in women, movable tender kidney, regarded by Haussmann as the commonest mistake, and adhesions following appendectomy. Cholelithiasis, pseudo-appendicitis, a very doubtful condition, and colica appendicularis, the correct diagnosis of which must require unusual skill, have also been mentioned by Fischler. The prognosis is usually favorable in the milder forms, at least death does not result, but some of the severer types of obstruction may lead to strangulation, peritonitis, and other grave complications, as in the cases reported by Wiemann, Heiler, and Straschenko.

The treatment is by no means definitely determined. Albu believes that internal measures, such as regulation of the diet, laxatives, massage of the abdomen, and prolonged rest, may be successful. Fischler advises a diet somewhat restricted and carefully adapted to the patient, massage, exercise to strengthen the abdominal muscles, and the administration of bismuth, combined, if necessary, with magnesia and rhubarb, or if there is diarrhea, bismuth salicylate may be used. Purgatives and oil and other enemas should be avoided.

The majority of writers, Haussmann, Wilms, Klose, regard surgery as the only satisfactory remedy. The nature of the operation is not settled. Wilms dissects upward a portion of the parietal peritoneum, leaving a pocket into which the cecum is sutured. Rehn and Klose simply attach the cecum to the lateral abdominal wall by sutures, securing a broad area of adhesions. This would seem sufficient in ordinary cases. As in all new operations for chronic conditions, the results are apparently uniformly favorable; at least, none that are unfavorable are reported, although Wilms speaks only in general terms, and Klose does not give the final results in all his cases.

I can easily understand why the fixation of the cecum should prevent recurrent attacks of colic, if they are due to temporary obstruction, but it is not clear to me why it should relieve a chronic constipation or restore the contractibility of an atonic colon, and, therefore, purely upon theoretical grounds, it would seem desirable at the time of the operation to correct all displacements, kinks, or folds that are giving rise, or may in the future give rise to partial or complete obstruction.

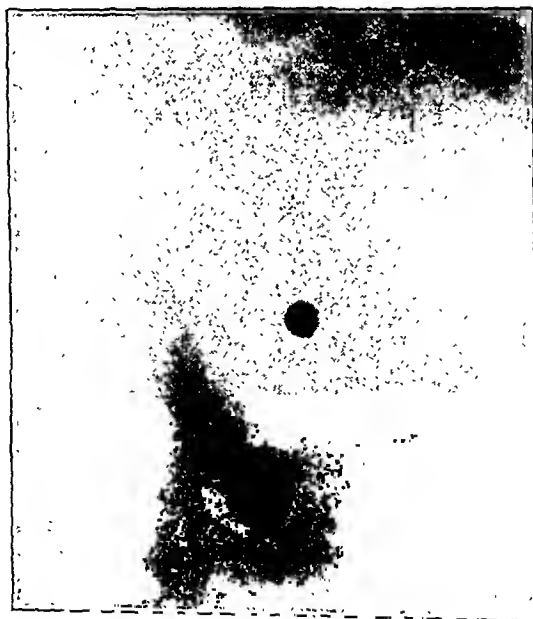
CASE I.—Miss E. H., three years ago complained of feeling in poor condition, sleeping badly, suffering from rumbling and flatus in the bowel. There was habitual constipation, only partly relieved



Left

Right

FIG. 1.—Case I. Two ounces of bismuth subcarbonate taken at 9 A.M. First exposure same day at 2.15 P.M. Plate shows a greatly distended and ptosed cecum, the lower end of the cecum being below the upper border of the symphysis. Some of the bismuth has also passed into the transverse colon which is lifted by the distended cecum. The bismuth has not quite reached the splenic flexure. There is no bismuth in the stomach and mere traces in the small intestines. Therefore the motility of the stomach and small intestines is normal.



Left

Right

FIG. 2.—Case I. Same patient. Picture taken at 9.15 A.M., two days later, without further ingestion of bismuth. There is still a slight accumulation of bismuth in the cecum. The main mass is in the transverse colon.

by laxatives. In the past she had had frequent vomiting. On the first examination it was noted that the heart and lungs were normal. There was some tympany on the right side of the abdomen, and peristalsis was diminished, but no tenderness was found. Various laxative remedies and diets were tried, and the patient's weight, originally about 130 pounds, increased steadily. Occasionally the cecum was palpable and gurgling was detected, but this was not invariably the case. The sigmoid flexure could also be felt from time to time as a firm cylindrical mass. About two years after the first visit, very distinct tenderness was elicited over McBurney's point. The ascending colon at this time was distinctly palpable, and was tender upon deep pressure without flinching or rigidity. She underwent then a course of massage, having been assured by the masseuse that her constipation would be relieved. This produced considerable pain in the right side of the abdomen, and occasionally some pain on the left, and the constipation was not improved. The diagnosis of chronic appendicitis was made, and as during this long period of treatment, although the patient had gained in weight, she had never been wholly well, her parents requested that an operation be performed. This was done by Dr. Martin in June, 1911. The appendix was free and easily removed, and the postoperative course was entirely normal. For a short time after this she seemed distinctly better, but by August was as bad as ever, tiring easily and being moderately anemic. The cecum could still be felt, and the lower end seemed to be about the level of the interspinal line. The patient at the last examination was improved somewhat in strength and weight, but the constipation with occasional periods of relief was practically unimproved. She was, therefore, referred to Dr. Pancoast for x-ray study. On October 9 two ounces of bismuth subcarbonate in suspension were given at 9 A.M. A picture was taken at 1 P.M., and showed that the stomach was empty and that a considerable amount of bismuth had already passed into the cecum. This confirmed the diagnosis of normal gastric and intestinal motility. On October 11, at 10 A.M., a second picture was taken, and it was found that the cecum still contained a considerable amount of bismuth. It was abnormally long, extending considerably below the interspinal line. There was marked ptosis, with festooning of the transverse colon (see Figs. 1 and 2).

CASE II.—Miss E. P., was first seen in February, 1908. At this time she was feeling miserably, and complained of headache and nausea in the morning, dyspnea on exertion, inability to pursue her work, some gas half an hour after eating, and occasional bloating. At the age of twenty she had had an attack diagnosed peritonitis. Thirteen years later, when the symptoms had persisted for years, the appendix was removed. Immediately after this operation she developed typhoid fever and was in bed seven

weeks. She had always been constipated, and since the onset of menstruation she has suffered from dysmenorrhea. At this time her weight, 161 pounds, was better than it ever had been previously. She is over six feet tall, however, and appeared poorly nourished. The abdomen was moderately tympanitic; there was considerable splashing in the stomach, and a good deal of tenderness over the right side of the abdomen and hyperesthesia in the same region. All the tendon reflexes were greatly exaggerated. The blood pressure was low. The patient stated that the ghost of her appendix had come back to haunt her, because there had been no relief from pain after the operation. The cecum was quite palpable, and from time to time gurgling was present. Considerable relief was given by the

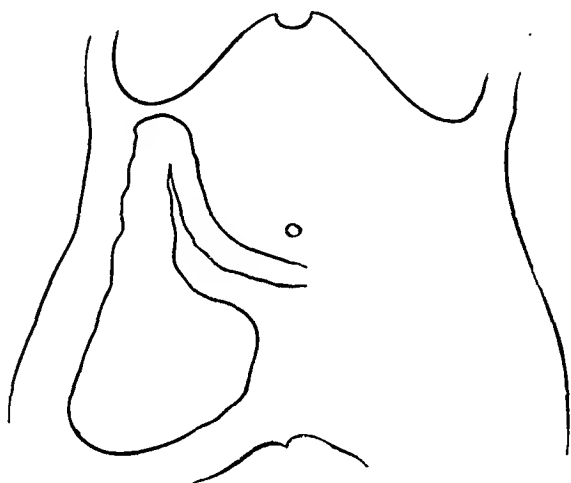


FIG. 3.—Case 11. But one plate was taken forty-eight hours after the ingestion of two ounces of bismuth subcarbonate. This plate was not sharp enough for correct reproduction and the outlines of the shadows could only be seen by holding it obliquely to the light. The sketch is an approximate reproduction of the shadow which indicates an enormous dilatation and retention in the cecum. The transverse colon is in good position and shows the permanent results of the Coffey operation done one and one-half years ago.

application of adhesive straps to relieve the ptosis of the colon, but the constipation was difficult to overcome. The patient slept badly and had vivid dreams. She steadily lost weight, and the marked persistence of the tenderness led finally to the decision to examine the lower end of the colon in order to find out whether adhesions or some other condition could account for her disability. This was done by Dr. Clark, who found a few adhesions, which he severed, and closed the wound. Recovery from the operation was uneventful, but the patient was unimproved. She then decided to spend the winter in Italy, in the hope of overcoming what one of her physicians believed to be a neurasthenic state. Unfortunately, she was in Sicily at the time of the earthquake, and believes that her failure to improve was due to the excitement of this period.

Upon her return a lump developed in the left breast, which was amputated by Dr. George Ross. Microscopic examination showed, however, that the tumor was a simple fibroma. Prolonged rest cure under favorable conditions failed to give any relief; indeed, the patient seemed to be worse, and in view of the profound ptosis of the colon shown by *x*-rays, it was finally decided, after several consultations, that Dr. Clark should again operate. This he did, resecting a considerable portion of the sigmoid flexure and performing Coffey's operation to relieve festooning of the transverse colon. This operation was only performed at the earnest request of the patient, who was willing to submit to anything in order to regain her health. There was no improvement, and the patient is now apparently a permanent invalid. The diagnosis is not definite, but I can recollect distinctly at the time of the second and fourth operations, at both of which I was present, that the cecum moved very freely, and was rather long and distinctly distended. This did not attract the attention of any of us at the time, but the history of the case, the prolonged constipation, the failure to improve after the removal of the appendix, the palpable colon, all lead me to conclude that part of her troubles are due to an unfixed cecum. The *x*-ray taken two days after the administration of two ounces of bismuth showed marked retention in the cecum (see Fig. 3).

CASE III.—M. R. B., was first seen in February, 1908. She was then a girl, aged fifteen years, who had been criminally overworked at school, being occupied from 6 A.M. until 8 P.M., and spending her recesses practising on the piano. As a child she had been well and strong. About the age of thirteen she began to have cramps in the abdomen. These would begin with severe pain in the right lower quadrant, and were sometimes associated with nausea and vomiting. As a rule, the attacks would last for twelve hours, then cease for two or three days. At first they recurred every two or three months, but later increased both in frequency and severity. In the intervals she suffered from a good deal of gas, nausea after food, and occasional vomiting. There was considerable tenderness over McBurney's point, and gurgling upon pressure on the cecum. Peristalsis appeared to be quite active on auscultation. The pulsation of the right common iliac could easily be felt. The patient complained of constipation, which was only relieved by large doses of purgative drugs. She was placed upon a rest cure, during which she gained some weight, but the constipation persisted in spite of all forms of treatment. During this time she seemed extraordinarily listless for a girl of her age, and I ascribed this to anemia, the red cells being 3,280,000. After this she steadily lost weight, going from 93 to 81 pounds. The tenderness in the right lower quadrant persisted. It was always worse during menstruation, and was supposed to be due to chronic appendicitis that was in part or

wholly the cause of the chronic constipation. Finally appendectomy was done by Dr. Edward Martin. The appendix was free. It showed slight signs of chronic inflammation. Recovery from the operation was prompt and satisfactory. There has been no improvement. The patient at various times has seen specialists in Europe, has undergone a course of osteopathy, and appears practically to have abandoned hope. No x-rays have been taken, but the history is typical. An occasionally palpable cecum with gurgling suggests very strongly that this is a case in which the movable cecum is accountable for the symptoms.

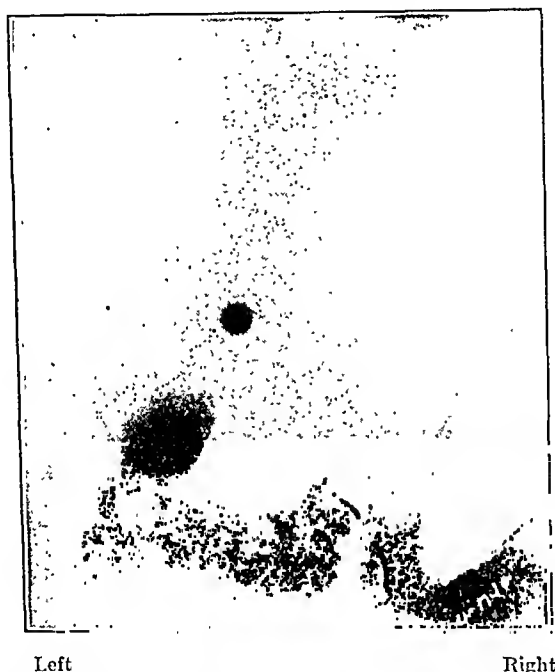


FIG. 4.—Case IV. Bismuth subcarbonate, two ounces, in suspension at 9 A.M. First picture 12.45 P.M. The stomach still contained a large amount of the bismuth which is shown clearly. It is below the umbilicus. The cecum was greatly ptosed and its shadow can be seen extending beneath the ramus of the pubic bone. The bismuth has not distinctly reached the transverse colon.

CASE IV.—Mrs. J. B. P. was referred to me by Dr. W. R. Nicholson. She came complaining of loud gurgling and discomfort in various parts of the abdomen, periods of obstinate constipation alternating with diarrhea, and always much mucus in the stools. The appetite was poor. Menstruation was normal. The weight, 105 pounds. The cecum was palpable as a somewhat irregular freely movable mass containing some small hard lumps and the lower edge was one inch below the interspinal line. The lower edge of the liver was palpable, but the right kidney and sigmoid flexure could not be felt. This condition has persisted for years. Laxatives seemed to have fairly good results, and the bowel movements became more regular.

The appetite was poor, and the weight failed to increase. The cecum continued tender, and there was some diffuse tenderness over the whole of the lower part of the abdomen. There has been no evidence of gastric retention. There was extraordinary improvement for a short time after the application of adhesive straps. Two ounces of bismuth were administered, and x-ray pictures taken four and fifty-two hours later. There was no evidence of retention in the stomach or small intestines, but marked evidence of retention in the cecum for a period in excess of forty-eight hours (see Figs. 4 and 5).

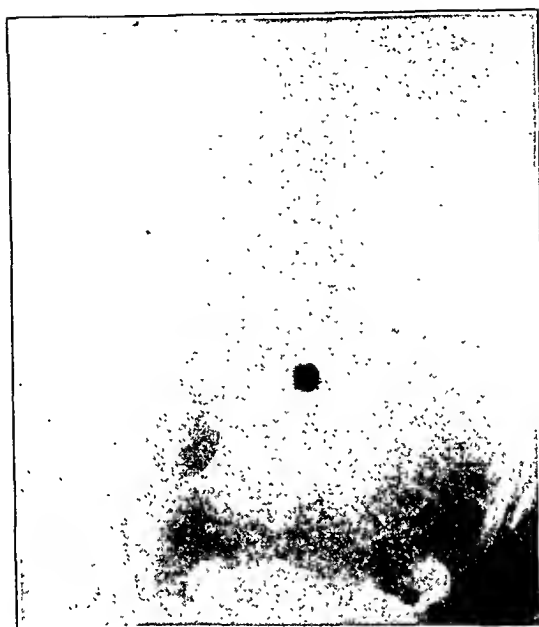


Left

Right

FIG. 5.—Case IV. Picture taken at 9.30 A.M. two days later. The cecum is still greatly distended with the bismuth and lifts the right side of the transverse colon which is festooned. The dilatation and motility of the cecum and ascending colon and an apparent obstruction at the splenic flexure all seem very distinct.

CASE V.—Miss A. G. C. was referred to me by Dr. Frank Craig. She complained of chronic constipation. Seven years ago she had had a slight attack of pulmonary tuberculosis, from which she had completely recovered. For two years the bowels have moved only after the administration of large doses of purgative medicine, particularly sulphate of magnesia. The feces often contain mucus, and sometimes blood. Seven years ago, after treatment for tuberculosis, she weighed 130 pounds. Her present weight is 104 pounds. The thoracic organs are normal. The cecum is distinctly palpable, the lower edge extending half an inch below the interspinal line, moves freely, but there is no gurgling and it is not tender. The sigmoid is palpable. The stomach is ptosed and atonic. Peristalsis



Left

Right

FIG. 6.—Case V. Bismuth taken at 9 A.M. First plate at 12.45 P.M. same day. Stomach is ptosed, somewhat sacculated, and lies far to the left and below level of the umbilicus. The cecum is ptosed and dilated. There are traces of bismuth in the small intestines and some has already passed into the transverse colon.



Left

Right

FIG. 7.—Case V. 9.30 A.M. two days later. Cecum is still considerably distended. There is also apparently considerable distention of the median portion of the transverse colon. Very little of the bismuth has been discharged.

is greatly diminished. The right kidney is in the fourth position. The patient was given bismuth and x-ray pictures were taken at intervals of four and fifty-two hours. These confirmed the physical examination, showing marked retention of bismuth in the cecum, and also in the large intestines (see Figs. 6 and 7).

No very definite conclusions can be drawn from this study. There seems to be no doubt that many cases are wrongly diagnosed chronic appendicitis, that in these cases the removal of the appendix, even if it shows signs of inflammation, is not followed by the relief of the symptoms, and, therefore, some other etiological factor must be active. In no less than 3 of the 5 cases I report the appendix had been removed, and in every instance described as the seat of a chronic inflammatory process, and yet in none of those 3 was there any relief afforded, and in 1 subsequent operations were equally futile.

Although a great deal of work has been done upon the various positions of the colon, the cecum and ascending colon have been, comparatively speaking, neglected. This is due in part to the striking displacements of the transverse colon and sigmoid flexure. Recently, during an autopsy upon a case of pleural effusion and myocarditis that had died in my wards at the Philadelphia Hospital, I asked the pathologist to examine the cecum, and he found that it was not attached to the abdominal wall until a point midway between its beginning and the hepatic flexure was reached, and that, moreover, the lower end was reflected backward for a distance of two inches and fastened by adhesions between the two surfaces of cecal peritoneum. This is only mentioned as an illustration of the ease with which these anomalies may be overlooked even by a very competent pathologist.

It seems to me likely that the essential lesion in these cases is the atony which results from the partial and occasional obstruction, and I am inclined to agree with Fischler that the term typhlatonia is better than cecum mobile, but the latter appears to be now established. The mere discovery that the cecum is palpable, movable and retains bismuth for too long a period should not be regarded as an adequate explanation for obscure abdominal symptoms unless all other conditions are excluded, and from the study of my own cases I am strongly inclined to believe that the displacements of other portions of the colon, the co-existence of a catarrhal colitis or an associated chronic appendicitis will be of importance in determining the indications for treatment.

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THE LUMBAR TYPE OF INTERMITTENT CLAUDICATION.

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THE peculiar and very characteristic vascular disturbance, described by Charcot,¹ in 1858, as *Intermittent Claudication* has attained a place of considerable importance in symptomatology during the last few years. At the present time, a number of clinical types are recognized, which receive their special and distinguishing characteristics from that portion of the arterial system which is involved—the tibial, brachial, coronary, mesenteric, cerebral, or spinal arteries.

Charcot's original observations were made upon cases in which the large arteries of the lower extremity were involved, with a resulting condition of intermittent limping; a state of weakness, painful cramps and paresthesia developing in the extremity while walking, disappearing after a brief period of rest (*paralysie douloureuse intermittente*).

The peculiar feature of this clinical picture was the intermittent character of the symptoms, their appearance only during muscular activity and their rapid disappearance in the passive state.

This unusual complex of symptoms attracted very little attention for many years and it was not until after the revival of the subject by Erb,² in 1898, that it began to receive general attention and interest. Erb demonstrated conclusively that symptoms of *claudication intermittente* occur not only with disease of the large arterial trunks, but that they result even more frequently from lesions in the smaller ramifications of the arterial tree, with corresponding changes in the pulsation of the pedal arteries.

These symptoms may accompany all the commoner forms of arterial disease, arteriosclerosis, senile calcification, obliterating endarteritis, acute arteritis. It is, however, not only the organic changes in the vessel walls, but an associated *vasomotor neurosis*, a tendency to vascular spasm, which narrows the lumen of the vessels and diminishes the flow of blood to the parts, with a resulting ischemia, which is the direct cause of the symptoms. The two chief factors, angiosclerosis and angioneurosis, are therefore usually combined, although Oppenheim recognizes a benign, purely functional type due to vascular spasm.

Once the symptom complex was established in the lower extremity (leg type), it was but natural that other groups of cases

¹ Claudication Intermittente, *Compt. Rend. et mém. de la Soc. de Biol.*, 1858, t. xii, p. 225.

² *Deut. Zeit. f. Nervenheilkunde*, 1898, Band xiii, S. 1.

should be differentiated and described as special types, corresponding to different portions of the arterial tree.

Oppenheim³ called attention to its occurrence in the upper extremity (arm type), and not a few cases of this kind have been described. In one case, in which both legs and an arm were affected, the tongue was similarly involved (Determann⁴).

Of great clinical importance are the various visceral types of the disease, such as occur with lesions of the coronary artery (angina pectoris of Potain) and of the mesenteric arteries (Ortner⁵). It has also been observed in the central artery of the retina (Rosenfeld⁶). Such a case has come under my own observation, in which the arterial spasm and resulting pallor could be seen with the ophthalmoscope.

The condition is by no means infrequent in the cerebral arteries, often as a symptom and precursor of thrombosis. Déjerine⁷ has recently given a graphic picture of intermittent claudication of the vessels of the spinal cord, with pain, weakness, and paresthesie of the lower extremities coming on during exertion and accompanied by exaggerated tendon reflexes, ankle clonus, and the Babinski reflex, all symptoms objective as well as subjective disappearing during rest.

The Lumbar Type of Intermittent Claudication. The type to which I desire to call attention may from its location in the lower portion of the back be termed the *lumbar type* of intermittent claudication. The nature of the symptoms and their intermittent character, occurring regularly during activity, ceasing always after a short rest, would exclude all other organic conditions save one of vascular origin.

It may be that some of the painful backs occurring in and after middle life, and regarded usually as rheumatic, may have a similar origin, cases in which the intermittent character of the symptoms is less clearly defined than the one which has come under my observation.

CASE REPORT. Mr. M. G., aged fifty-one years, unmarried, a stockbroker by occupation, was referred to me from the Roosevelt Hospital in November, 1910. He is American born and has always lived in New York. For many years he has indulged excessively in the use of alcohol, usually whisky; on the average taking from ten to fifteen drinks a day, with not infrequent periods of debauch, during which times he would consume a quart of whisky a day, often for a period of several weeks. In addition to alcoholic excesses he is a heavy eater, and for many years has indulged in large quantities of rich food. For twenty years he has not used tobacco in any form. Twenty years ago he acquired

³ Deut. Zeit. f. Nervenheilkunde, 1900, Band xvii.

⁵ Wien. klin. Woch., 1906.

⁷ Rev. Neurologique, 1906, No. 8.

⁴ Ibid., 1907, Band xxii, S. 154.

⁶ Deut. med. Woch., 1906

sypilis, for which he received thorough treatment under the direction of a well-known New York specialist. Fifteen years ago he had a severe attack of articular rheumatism, but has had no rheumatic manifestations since that time. Has never had lumbago.

The trouble for which he consulted me began two years ago with pain in the lower part of the back, which came on only while walking. It was his custom at that time, and had been for some years, to walk to and from his place of business. He found that during these walks a pain would appear in the lumbar region and he would have to stand still a few minutes until it wore off. After standing a few minutes, usually leaning heavily against a fence or a lamp post so as to take "the weight and strain off the spine," as he expressed it, the pain would entirely disappear and he could resume his walk. While sitting, lying in bed, or on first rising in the morning, there was not a trace of pain or stiffness in the back. It developed only during his walk to the office.

As time went on he found it necessary to take more and more frequent rests, but always with the same result, a complete disappearance of the pain and perfect ability to continue his walk. In resting, it was necessary to take the strain off the muscles of the back by sitting, lying down, or, as was more frequently the case while walking, by leaning up against some object for support. He had no pain or trouble of any kind in the lower extremities. The pain was fairly well localized in the lower lumbar region and when very severe would radiate somewhat into the sides but never as far forward as the abdomen. The pain was intensely aching in character, and if he attempted to continue walking after its appearance it would develop into a painful, cramp-like feeling in the small of the back which would bring him to an abrupt standstill. After a short rest with support the pain and cramp would fade away entirely. At the time of his first visit to me he could walk about half a mile before the pain became severe. If he walked fast it came on more quickly. He had already undergone various treatments for chronic rheumatism, but without any amelioration of his symptoms, indeed they seemed to have grown worse instead of better.

Examination. November 1, 1910. He is a large, heavily built man, weighing 250 pounds stripped, there having been a steady increase in weight during the last fifteen years. The abdomen is large and pendulous, so that in standing the shoulders are thrown backward and the spine is arched posteriorly in order to maintain the equilibrium, and evidently throwing a considerable strain on the lower portion of the erector spinæ group of muscles. The movements of the spinal column are perfectly flexible in all directions and cause no pain whatever. There is no trace of tenderness on direct pressure over the spine or over the muscles of the lumbar region. Jarring of the spine is equally negative.

The pupillary and tendon reflexes are normal. Indeed, except for a slight tremor of the hands and the mental and physical stigmata of chronic alcoholism, my neurological examination was negative.

The heart sounds were free from murmurs and the pulse was of moderate tension.

The femorals, popliteals, and pedal arteries were palpable. There was not, nor had there been, any swelling or edema of the feet or legs. The urine was free from albumin and sugar.

REMARKS. From the symptoms presented by this patient, I think there can be little doubt but that we are dealing with the very characteristic condition of intermittent claudication manifesting itself in the lower portion of the sacrolumbar mass.

The man never experienced the slightest discomfort while in bed or when sitting. Walking or long-continued standing alone brought on the pain, which was deep-seated and very intense, and was always relieved by support of the spine, which removed the strain from the affected muscles.

The condition had persisted for two years, gradually growing worse in spite of treatment. The spine was perfectly mobile and the painful area was not tender on pressure.

This region receives its arterial blood supply through the lumbar arteries, which are four in number and arise at right angles to the abdominal aorta. Occasionally they take their origin from a common trunk, which subdivides into a right and left lumbar artery. The lumbar arteries then course between the psoas magnus muscle and the vertebral column to the interval between the transverse processes, where a division takes place into a dorsal and an abdominal branch, similar to the divisions of the intercostal arteries.

The dorsal branch gives off immediately after its origin a spinal branch, which enters the spinal canal and is distributed to the spinal cord; it then continues its course backward between the transverse processes and is distributed to the muscles and integument of the back, anastomosing with branches of the adjacent lumbar arteries.

The abdominal branch passes outward behind the quadratus lumborum and is continued between the abdominal muscles, anastomosing with the epigastric and internal mammary arteries in part.

As the symptoms in the case are limited to the lumbosacral region, occasionally extending into the sides, I would attribute them to disease of one or more of the lumbar arteries or to an arteriosclerotic process in the abdominal aorta, which interferes with the free flow of blood through these vessels, so that a sufficient blood supply is received for the physiological processes in the passive state, but which does not suffice for the increased demands

of the sacrolumbar mass during activity, hence the painful cramp and its peculiar intermittent character. I have found no cases recorded of intermittent claudication of the lumbar region, nor have I observed a similar case. It seems to me, however, not improbable that other cases of this same type may occur and have been overlooked or misinterpreted and that some of the lumbar pains and cramps of advanced life may be dependent upon arteriosclerotic processes in the abdominal aorta or its lumbar branches.

ACUTE YELLOW ATROPHY OF THE LIVER IN CHILDREN, WITH REPORT OF A CASE.

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ACUTE yellow atrophy of the liver is a very rare disease. In fact, Osler¹ states in the third edition of his *Practice of Medicine* that he had never seen a case. Rolleston,² in twenty years had seen in the postmortem room or examined the liver of 7 cases. It occurs much less frequently in children than in adults, and for that reason the following case is considered worthy of report.

G. R., a female child, aged five years, was admitted to the children's ward of Lakeside Hospital, November 3, 1909, suffering from intense jaundice associated with stupor. Neither the family nor the personal history threw any light on the case. One week before admission she began to lose her appetite, and vomited several times a day, the last time she vomited being two days before coming to the hospital. During this time the child became more deeply jaundiced, the stools were clay colored, and the urine a deep yellow color. The parents stated that they had not noticed any blood in the vomitus or in the stools. During the last twenty-four hours she had been unconscious.

Physical examination showed a well-developed and quite well-nourished child, tossing about restlessly in bed. The skin and mucous membranes were deeply jaundiced, a small ecchymotic area was noticed in the left lower quadrant of the abdomen, and another on the outer side of the right arm just above the elbow. There were numerous small petechiæ over the lower extremities below the knees. The child was unconscious, but seemed hypersensitive when touched. The pupils were widely dilated and reacted sluggishly to light. The ears, nose, and throat were normal, but

¹ *Practice of Medicine*, 3d ed.

² *Diseases of the Liver, Gall-bladder, and Bile-ducts*, 1905.

the tongue was heavily coated with a yellowish-white fur. Slight general glandular enlargement was noted. The temperature was 96.2° by rectum, the respirations were 30 to the minute, and somewhat shallow and irregular. Examination of the lungs revealed nothing abnormal. The pulse rate was 64; with the exception of some arrhythmia there was nothing of importance in the examination of the heart. The abdomen was somewhat distended, especially in the lower part, this being due to a full bladder. The spleen could be felt. The lower edge of the liver was not palpable; the upper border of hepatic dulness began at the fourth rib in the right mammary line, and at the sixth rib in the axillary line. The tendon reflexes were exaggerated, and there was some spasticity of the legs. The urine was dark yellow in color; specific gravity, 1017; alkaline, contained a faint trace of albumin, and bile was present in large quantity. The microscopic examination of the centrifugalized sediment showed many epithelial and hyaline casts and many leucin crystals. The leukocyte count was 22,400.

The child vomited shortly after admission to the hospital, the vomitus being mixed with dark clotted blood. The stomach was then washed out and numerous blood clots came away in the washing. The child died two hours later.

AUTOPSY REPORT. *Anatomical Diagnosis.* Acute yellow atrophy of the liver, icterus, petechial hemorrhages (skin, omentum, mesentery, mediastinal tissues, epicardium, pleura, lung, Peyer's patches, mucous membrane of the stomach), cloudy swelling of heart, kidney, pancreas, and adrenals, stenosis of the cystic duct, thyroid hyperplasia.

Autopsy was performed nine hours after death. The body was that of a well-formed female child, 95 cm. in length. Postmortem rigidity was slight. There was marked postmortem staining over the dependent parts, with numerous petechial spots on the extremities below the knees. The skin everywhere was markedly icteric, the conjunctivæ bright yellow, the pupils widely dilated and equal. A dark brownish fluid was exuding from both nostrils; the ears were free from discharge. The superficial fat was moderate in amount and bright yellow in color.

The peritoneum was smooth. The fat everywhere, omental, mesenteric, and in appendices epiploicæ, showed numerous hemorrhages varying in size from a pin head to a dime. The hemorrhagic condition in the mesentery was very striking, and seemed to be equally distributed throughout, being most marked toward the attachment to the gut. The liver was small, pale in color, its lower border lying well above the margin of the ribs. The gall-bladder, ducts, and the appendix appeared normal. There was a small amount of free bile-stained fluid in the peritoneal cavity. There was nothing abnormal about the diaphragm.

Both pleural cavities were free from adhesions, and contained

a small amount of bile-stained fluid. Beneath the visceral pleura, numerous small hemorrhagic points were noted; these were also quite numerous in the mediastinal fat and in the fat of the epicardium. The pericardium contained a small amount of bile-stained fluid; there were no adhesions, and no subpericardial hemorrhages. The heart weighed 70 grams. The valves were normal; the endocardium was bile stained, but there were no hemorrhages beneath it.

The right lung weighed 170 grams, crepitant and air containing throughout. The surface was smooth and mottled with small dark red areas. On section throughout the lung substance, varying in size from a pin point to 2 cm. in diameter, were numerous small hemorrhages; the bronchial mucosa was slightly congested. The left lung weighed 160 grams, and showed the same conditions as the right except that the hemorrhagic areas were more numerous. The bronchial lymph glands were not enlarged.

The colon was normal. The ileum showed nothing of note except a hemorrhagic Peyer's patch just above the ileocecal valve. The duodenum showed some congestion just above the papilla of the common bile duct. The bile ducts were normal with the exception of the cystic duct, which was occluded 2 cm. from its origin in the gall-bladder. The walls of the stomach were covered with a large amount of thick mucus, and there were a few small hemorrhages into the mucosa along the greater curvature.

The liver weighed 250 grams, was pale in color, very flabby, and showed some wrinkling of its capsule. It lacked the rigidity of a normal liver, and partially collapsed and bent under its own weight. On section, the lobular markings were indistinct, and showed bright yellow areas 1 to 2 cm. in diameter, mingled with reddish slightly depressed areas. The outlines of the lobules were entirely lost in the red and could only occasionally be discerned in the yellow areas. The gall-bladder contained a small amount of bright yellow mucus, and the walls were slightly congested. The pancreas was normal.

The right kidney weighed 80 grams. The capsule stripped readily, leaving a smooth surface, fetal lobulation was well marked. On section, the cortex was swollen, and showed marked cloudy swelling. The left weighed 75 grams and was similar to the right.

The thymus was normal. The thyroid was slightly enlarged. The trachea and larynx showed no submucous hemorrhages.

The brain weighed 1075 grams. The calvarium showed marked depressions, every convolution of the cerebrum being marked by a corresponding mould in the inner table of the skull. The dura mater showed definite bile staining. The section of the brain showed nothing unusual.

On microscopic examination, the liver showed extensive degeneration. In many sections no trace of liver cells could be seen,

nothing being left but the vascular stroma. In other sections traces of liver cells still remained, but the cells were granular, vacuolated, and stained diffusely; an occasional cell could be seen which stained well, these having a granular vacuolated cytoplasm and a small darkly stained nucleus. There was no evidence anywhere of regeneration of liver cells. In the areas where the degeneration of liver tissue was most marked, the capillaries were distended with blood. Hemorrhages were quite numerous. The interlobular bile ducts showed everywhere a marked proliferation; this was most marked in the areas where the destruction of the liver cells was greatest. Here the lobules were completely surrounded by proliferated connective-tissue of Glisson's capsule in which were numerous newly formed bile ducts. These showed a tendency to spread down into the lobules in places, which was evidently an attempt at regeneration. Glisson's capsule showed a slight rounded infiltration, and was everywhere thickened, in some places considerably so. The gall-bladder was normal; desquamated epithelial cells filled the lumen of the bile ducts. The heart showed nothing but a considerable grade of cloudy swelling. In the lungs a few small areas of focal hemorrhage were seen. There was nothing else abnormal. The thymus was normal. The thyroid showed a moderate grade of hyperplasia. A moderate degree of cloudy swelling was found in the adrenals. The brain was normal.

Cultures taken from the heart blood gave a pure growth of *staphylococcus albus*. Sections of the liver stained by the Levaditi method failed to show spirochetes.

In 1894 William Hunter was able to find 250 published cases of acute yellow atrophy of the liver. Four years later McPhedran³ collected 29 additional cases. In 1903 Best,⁴ in an exhaustive study, found about 500 cases reported in the literature. Of these, a small proportion occurred early in life. I have been able to find reports of 40 children with this disease; these including my own patient making a total of 41. In 1905 Rolleston was able to collect 22 cases in the first ten years of life.

One of the earliest cases recorded was that of Politzer,⁵ who, in 1858, observed this condition in a newborn infant. On the fourth day after birth the child became ill with jaundice and bloody vomit, which became worse on the following day, and was accompanied by high fever and restlessness with a tendency to stupor. Later the left lobe of the liver showed a perceptible diminution in size. On the eighteenth day the child died, death being preceded by convulsions and bleeding from the umbilicus. The urine showed leucin and tyrosin crystals. The liver at autopsy was considerably diminished in size, the diminution chiefly affecting the left lobe. The bile passages were patent and the umbilical veins and arteries

³ Sajous' Annual, 1899, iv. 393.

⁵ Jahrb. f. Kinderneilkunde, 1860.

⁴ Thesis, Univ. of Chicago, 1903.

were normal. The microscopic examination of the liver showed a high degree of destruction of the liver cells. The same author, two years later reported a case in a girl baby four months old, who became suddenly ill with diarrhea, vomiting, and fever, the symptoms suggesting a gastro-intestinal catarrh. On the seventh day of the illness, icterus appeared, which became very intense. The stools were free from bile pigment. The liver was enlarged and painful on pressure. This increased liver dulness continued until the twelfth day. On the fourteenth day there was evident diminution in the size of the liver, blood was vomited and passed with the stools. Forty-eight hours later the child died from exhaustion, and by this time no liver dulness could be made out below the costal margin. An autopsy showed that the liver was small and flabby, and microscopically there was great destruction of liver cells, the latter containing a great deal of fat.

The following cases have been reported by various authors: Loeschner,⁶ boy, aged three years; Mettenheimer,⁷ boy, aged four years; Widerhofer,⁸ girl, aged one and three-fourths years; Hecker,⁹ newborn girl; Senator,¹⁰ girl, aged eight months; Brandenburg,¹¹ boy, aged eleven weeks; Hilton-Fagge,¹² boy, aged two and one-half years; Steiner,¹³ boy, aged ten years; Monti,¹⁴ boy, aged four years; Pleischl and Falwarczny,¹⁵ boy, aged fourteen years; Mann,¹⁶ boy, aged one and one-fourth years; Aufrecht,¹⁷ newborn child, Dinkler,¹⁸ girl, aged twelve years; Brunton and Tunnicliffe,¹⁹ boy, aged three and one-half years; Foltanek,²⁰ boy, aged twelve years; Goodhart,²¹ boy, aged two and one-half years; Bjelin,²² child, aged thirteen years; Greves,²³ child, aged one and three-fourths years; Babes,²⁴ boy, aged six years; Lewitsky and Brodowsky,²⁵ child, aged fifteen years; Lanz,²⁶ boy, aged four years; Meder,²⁷ boy, aged fifteen years; Merkel,²⁸ boy, aged six years; Poddig,²⁹ boy, aged two and one-half years; Rehn and Perlo,³⁰ boy, aged two and one-half years; Rinsema,³¹ girl, aged five years; Rosenheim,³² girl,

⁶ Oesterreichische Zeits. f. Kinderheilkunde, 1856. (Abstract, British and Foreign Medico Chirurg. Review, 1860, vol. xxv.

⁷ Memorab. aus der Praxis., 1862, vol. vii.

⁸ Jahrb. f. Kinderheilkunde, 1859, Band ii, p. 42.

⁹ Monatssch. f. Geburtskunde, 1867.

¹⁰ Jahrb. f. Kinderheilkunde, 1865.

¹¹ Festschrift f. e. Hagenbach-Burekhardt, Basel, Leipzig, 1897, S. 61.

¹² Trans. Path. Soc., London, 1869, xx, 212.

¹³ Jahrb. f. Kinderheilkunde, 1871, S. 428.

¹⁴ Archiv f. Kinderheilkunde, Band vii, S. 346.

¹⁵ Zeits. der K. K. Gesell. der ärzte zu Wien, 1858.

¹⁶ Amer. Jour. Obstet., 1875, viii, 539.

¹⁷ Zentralbl. f. innere Med., 1896, No. 2.

¹⁸ Inaug. Dissert. Halle, 1887.

¹⁹ St. Barthol. Hosp. Rep., 1896, xxxii, 425.

²⁰ Quoted by Merkel.

²¹ Trans. Path. Soc., London, vol. xxxiii, p. 82.

²² Quoted by Merkel.

²³ Brit. Med. Jour., 1884, i, 766.

²⁴ Virchow's Archiv, 1894, No. 136.

²⁵ Quoted by Merkel.

²⁶ Wien. klin. Woch., 1896.

²⁷ Ziegler's Beiträge z. Path. Anat., 1895, Band xvii, S. 143.

²⁸ Münch. med. Woch., January 30, 1904.

²⁹ Inaug. Dissert. Königsberg, 1892.

³⁰ Berl. klin. Woch., 1875, S. 644.

³¹ Quoted by Merkel.

³² Zeits. f. klin. Med., 1889, Band xv.

aged ten years; Heukelon,³³ child aged three months; Starek³⁴, boy, aged two and one-half years; West,³⁵ boy, aged six years; Schmidt,³⁶ boy, aged two and one-fourth years; Todt,³⁷ girl, aged three and one-half years; Carpenter,³⁸ girl, aged twenty-three months; Rogers,³⁹ boy, aged four years; Parkinson,⁴⁰ boy, aged four years; Wentworth,⁴¹ boy, aged five years; Griffith,⁴² boy, aged seven years; Drennan,⁴³ boy, aged eight years. The proportion of boys and girls afflicted is approximately two to one.

The etiology of acute yellow atrophy of the liver is quite unknown, but it is probably not due to a specific poison, for we find that numerous forms of intoxication, particularly chloroform, phosphorus, syphilis, alcohol, puerperal eclampsia, may lead to a condition closely resembling this disease. I have seen one case of chloroform poisoning in which the symptoms and the course of the disease were indistinguishable from acute yellow atrophy of the liver, and leucin and tyrosin crystals were found in the urine. Inasmuch as there is such a marked resemblance between this disease and phosphorus poisoning, some writers have thought that all cases were due to poisoning with phosphorus, but that is not true, as recent pathological studies have served to differentiate between the two conditions. Wells⁴⁴ has summarized the chief differences between phosphorus poisoning and acute yellow atrophy as follows: "Phosphorus produces a general injurious effect upon all the organs of the body, the liver merely showing the most marked anatomical changes, which at first consist of fatty metamorphosis of the liver, due to a migration of the body fat from the fat deposits into the injured cells, subsequently the liver cells disintegrate, the cytoplasm being affected before the nucleus, and the liver may become smaller than normal, although it is usually enlarged because of the fat deposition. Typical acute yellow atrophy is characterized by an early necrosis of a large proportion of the liver cells, the nucleus becoming unstainable while the cytoplasm is still little altered in appearance, and fatty changes play a subordinate role or are absent. As Auschutz says, "The poison seems to strike at the life of the cell, its nucleus, while phosphorus attacks the cytoplasm. Furthermore, the poison of yellow atrophy seems to be very specific, for it attacks the other organs of the body almost not at all, and within the liver it affects only the hepatic cells proper, while the bile duct

³³ Nederl. Tijdschr. v. Geneesk., 1888.

³⁴ Jahrb. f. Heilkunde, 1898.

³⁵ Trans. Path. Soc., London, 1880, xxxi, 116.

³⁶ Inaug. Dissert. Kiel, 1897.

³⁷ Akute gelbe Leberatrophie im kindlichen Lebensalter, Berlin, 1903, p. 32.

³⁸ Reports of Soc. for Study of Disease in Children, London, v, 133, 134.

³⁹ Reports of Soc. for Diseases in Children, 1906, vi, 294.

⁴⁰ Report of Soc. for Study of Disease in Children, London, 1906, vi, 229.

⁴¹ Archives of Pediatrics, February, 1906, p. 81.

⁴² Archives of Pediatrics, February, 1906, p. 88.

⁴³ Jour. of Path. and Bact., July, 1911, p. 141.

⁴⁴ Chemical Pathology, 1907.

epithelium and stroma cells are so little injured that they are able to proliferate greatly, this proliferation being a prominent feature." Wells further considers that the atrophy is due to an autolysis of necrotic liver cells by their own enzymes, and that in the most typical cases of acute yellow atrophy we have to do with a poison having a very specific effect on the liver cells, which destroys their synthetic activities without injuring their intracellular proteolytic enzymes, and consequently autolysis occurs. The fact that so many cases are preceded by symptoms of gastro-intestinal disturbance would lead us to suppose that this poison was of intestinal origin. Quincke considered that possibly regurgitation of pancreatic juice up the bile ducts might be responsible for the degenerative condition in the liver, but this is not true, for the bile pressure is greater than that of the pancreatic juice, and the bile ducts and peripheral portions of the lobules are always least affected. Klebs, Eppinger, and others have ascribed a bacterial origin to this disease, basing their conclusions on the finding of bacteria in the bile ducts and liver detritus in fatal cases. The bacteria in these cases were probably secondary invaders. In a case reported by Aufrecht, the disease in a newborn infant was associated with a *sclerema neonatorum*.

Acute yellow atrophy may occur in chronic drunkards, the condition supervening on existing cirrhosis. It may also occur in secondary syphilis. In a case reported by Merkel, though the child showed no signs of syphilis, the father had a syphilitic spastic paralysis of the lower extremities, and the mother had had repeated abortions. The disease is commonest between the ages of twenty and thirty in adults, females being more often attacked than males, in the proportion of 2 to 1, in contrast to the condition we see in children, where males are more frequently affected.

The majority of cases run their course in two weeks. Occasional cases occur in which the disease is spread over many weeks or months. In general we can divide the symptoms into two stages. The first, which lasts five or six days or sometimes much longer, is characterized by malaise, often muscular pains, nausea, vomiting and occasionally diarrhea, at other times constipation. The jaundice appears during the latter part of this stage. Often the jaundice is the first sign, increasing steadily in its intensity. Cases of acute yellow atrophy have been described in which no jaundice was present.

The second stage is marked by the pronounced grave change in the patient's condition, and especially by the appearance of nervous symptoms, severe headache, intolerance of light, restlessness, delirium, twitching of the muscles, convulsions, coma. In this stage transient paralyses sometimes occur, so that, excluding the jaundice, the clinical manifestations may closely resemble meningitis.

With the onset of the second stage the vomiting becomes more severe and the vomitus often contains blood. The tongue is dry, brown, and tremulous, and the teeth covered with sordes. The pulse is rapid and of low tension. The respirations are often quite irregular. The temperature is often elevated; in other cases it is depressed, rising just before death. Often petechiæ and hemorrhages are found beneath the skin, and blood may be passed in the stools and urine. Epistaxis occasionally occurs. The liver at first may be increased in size, but, as a rule, the liver dulness is much diminished before death, this diminution being partly due to the change in size of the organ and partly to its flabbiness, allowing it to fall away from the abdominal wall, the coils of intestine taking its place. The spleen is sometimes enlarged. The urine contains a great deal of bile and, as a rule, albumin and casts. It is remarkable that glycosuria is not observed. The urea is diminished, but the percentage of nitrogen present as ammonia is increased. Leucin and tyrosin are nearly always present, sometimes one being present in the urine without the other. There is nothing distinctive about the blood. Leukoeytosis is nearly always present, and in a few cases colon bacilli have been found by blood cultures. The coagulability of the blood is decreased.

Morbid Anatomy. The liver is always greatly diminished in size, often weighing only one-half to one-third of the normal weight. The liver is more or less universally affected, but often the left lobe shows the most marked atrophy, as in the first case reported by Politzer. In the chronic cases where the disease has existed for months the surface of the liver, instead of being smooth, is nodular, due to a compensatory hyperplasia of the liver cells, comparable to the adenomata seen in cirrhosis. The capsule is wrinkled and loose, and small hemorrhages may be seen beneath it. The liver is flabby, so that it bends readily under its own weight. Its surface is greenish yellow in color, with here and there reddish areas. It cuts with resistance. The cut surface is a bright lemon-yellow color, with numerous patches of darker brownish red, the latter predominating in the left lobe, where the greatest atrophy is seen. The yellow areas are soft and slightly swollen, the reddish areas are tough and of a leathery consistency. Histologically the change in the yellow areas are seen to be more recent, the parenchymatous cells showing extensive fatty changes, the fat droplets being within the nucleus, as well as within the cytoplasm. In the red areas, absorption of the fatty material has taken place, and we see mainly a network of capillaries, within the meshes of which are degenerated liver cells and the detritus of broken-down liver cells, masses of chromatin, and blood. When death has been delayed, evidence of regeneration can be seen in the form of patches of newly-formed liver cells, with deeply staining nuclei, some of them exhibiting mitoses. Pseudo-bile capillaries may also be present in con-

siderable number. Crystals of leucin and tyrosin may be seen in fresh sections, and the amount of fat which can be extracted from the liver is about 5 per cent. above the normal. The gall-bladder contains bile mixed with a great deal of mucus, and the bile ducts are normal.

The kidneys and heart show evidences of cloudy swelling, and the spleen is softened and enlarged.

The gastro-intestinal tract usually shows evidences of catarrhal inflammation. There is often some ascites.

Petechial hemorrhages may be found beneath the pleura and pericardium, and in the intestinal mucosa, and sometimes extensive cerebral and meningeal hemorrhages occur.

The diagnosis is usually simple from the intense jaundice, the nervous symptoms, the atrophy of the liver and the finding of leucin and tyrosin crystals in the urine. The latter are sometimes seen in other conditions of the liver, where there are marked degenerative changes. Sometimes these cases are confused with cases of phosphorus poisoning, but a careful history will serve to distinguish the latter. Hilton-Fagge has recorded a case in a boy, aged two and one-half years, where the symptoms were incorrectly thought to be due to belladonna poisoning.

Acute yellow atrophy of the liver is almost uniformly fatal. A few cases of undoubted recovery have been recorded. In 1897 Wickham Legg gave a list of 28 reported cases of recovery.

There is no treatment of much avail. Free purgation, intravenous or subcutaneous transfusion with saline solution, and intestinal antiseptics have been recommended.

TREATMENT OF NOCTURNAL ENURESIS IN CHILDREN.

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NOCTURNAL incontinence of urine in children is one of the common and one of the most troublesome conditions which the physician is called upon to treat. It is perhaps for this reason that it is so commonly neglected both by the profession and by the laity. The physician after one or two therapeutic ventures dismisses the case with the suggestion that the adenoids should be removed, or, if it is a boy, that he be circumcised, and then if these suggestions are carried out and a cure does not result the family of the child become resigned to what they regard as inevitable.

If we exclude at the outset those cases in which there is evi-

dence of mental deficiency and those caused by congenital malformations, we have a group of cases which were formerly regarded as "essential" or idiopathic enuresis. As our knowledge of the subject has increased, the idiopathic cases have gradually diminished in number, and Bazy aptly remarked that essential enuresis means essential ignorance.

Enuresis is a symptom, and the underlying cause should be diligently sought. From the articles on the subject one gathers that many authors have theories which their statistics prove to be correct, and one is reminded of the blind men and the elephant.

In the first place, some of the children who suffer from enuresis have imperfect or undeveloped spinal cords. The diagnosis in these cases can only be suspected, but perhaps the main test is that these are the cases which resist treatment and which persist throughout life. Some of the individuals may show other signs of physical degeneracy, some do not.

Frankl-Hochwart has noted the fact that many adults suffering from neurasthenia give the history of enuresis in childhood.

Certain cases are apparently of an epileptoid character and Pfister¹ believes that those cases in which enuresis first manifests itself after five years of age, and in which the symptom is not constant but comes on at intervals, belong to this class.

Many children with enuresis suffer from an overirritable nervous system, and this may account for small lesions causing the urine to be passed through reflex irritability. In other cases the irritating lesion is marked and would affect the nervous system of the normal child.

Vulvitis and vaginitis in girls and urethritis and balanitis in boys are among the most common reflex causes of enuresis. The seat of the irritation may be in the rectum, and a polypus, fissure, or ulcer may be the unsuspected cause, or perhaps much more frequently infection with the oxyuris. Calculi, tuberculosis of the bladder, and vesical polypi may be mentioned as some of the causes. Hypertrophy of the bladder has also been met with. The drinking of too much fluid, especially in the evening, or the habitual eating of salty or other food causing thirst should be borne in mind.

Bed wetting may result from mere laziness, and in other instances a child may sleep so soundly that the warning of the distended bladder is unheeded.

Another cause is abnormal muscle tone, and Merklen² considers enuresis an element of weak motor inhibition.

In 1893, Freund³ mentioned the fact that in about one-half of the sufferers from incontinence of urine there existed a hyper-

¹ Monatsschrift f. Psychologie u. Neurologie, 1905, xv, 113.

² Bulletins de Société de Pédiatrie de Paris, June, 1909, p. 339.

³ Neurologische Zentralbl., November 1, 1893.

tonia of the muscles of the legs, and he therefore attributed the increased micturition to an exaggeration of the vesical tone. This conception of the disease has never met with any great recognition by clinicians. In order to get some information concerning the condition, Merklen studied 164 children between the ages of three and fifteen years in various stages of intellectual development, but the number did not include any idiots. In 116 the muscles were normal, and in 48 they were weak. The 116 normal children included only 8 who suffered from enuresis, while the 48 weak ones included 18, or a proportion of 6.8 per cent., as compared with 37 per cent. In the 26 children who had enuresis the ages varied from four to fourteen years. Looking at the problem from this standpoint, 69 per cent. showed motor weakness of the muscles.

Merklen calls attention to the fact that in these children cataleptoid attitudes are more frequent than among normal children.

It has long been known that children with adenoids are liable to suffer from enuresis. Fisher operated on 716 cases, and of these, 106, or 14.8 per cent., had enuresis. Mygin in 400 cases found 31 cases, or 7.75 per cent. Gruback in 427 cases found 61 with enuresis, or 14.28 per cent. On the other hand, Lilang examined 50 children with enuresis, and found only 8 who had adenoids. He operated on these and only cured one.

Allaria⁴ reported 22 cases, of which 8 were cured, 3 improved, 9 not improved, and 2 cured spontaneously. Of the 8 cases which were not cured, 1 had a rectal papilloma, 3 showed signs of mental degeneration, and these sometimes had incontinence of the feces due to a weak sphincter.

Kapsaun reported 35 cases, all cures, and in a second series of 20 cases 15 were cured and 5 improved, and Cautas in 15 cases cured 13, and the remaining 2 were improved. These latter statistics are so favorable that one is inclined to believe that there must be some error in them.

Williams has written several articles on the subject of enuresis, and he has found a certain class of cases which may briefly be described as follows:

These children suffer with subnormal temperature, with a usual range of from 96.2° to 97.2° F., and in some cases the temperature is even lower than this. They complain of being cold, even though they may be somewhat overclothed, and they often have what is popularly spoken of as "dead fingers"—that is, one or more fingers become blanched and very cold when the child is exposed to cold and often at other times. These children feel cold even in summer, and suffer more at night than during the day. They are also undersized and under weight. About one-

⁴ *Gazetta degli Ospedali et delle Cliniche*, April 27, 1909, p. 529.

half the cases have adenoids, but the nasal respiration is perfectly free. The high arched palate is present in all these cases, and Williams believes that all these things taken together indicate a thyroid insufficiency.

It is generally admitted that one of the functions of the thyroid secretion is to fix the calcium salts in the tissues, and that without a sufficient amount of secretion the salts cannot be utilized and bone formation is defective and the child fails to grow normally. He believes that the change in the shape of the bones is due to the fact that the bones are softer, without sufficient calcium salts, and so are more easily affected by pressure. Williams believes that the factor that decides the difference between the results of thyroid insufficiency in adults and the same insufficiency in children is the fact that the needs for the salts of calcium at the two periods of life are widely different.

Hertoghe⁵ has called attention to certain cases of myxedema fruste in childhood, in which nocturnal enuresis was mentioned as one of the symptoms. In this connection it is interesting to note that Léopold Lévi and H. de Rothschild have called attention to another sign of thyroid insufficiency, which they call the eyebrow sign (*signe de sourcil*). It consists in the lessening in the amount of the outer third of the eyebrow and sometimes in complete absence of this. Whenever this sign exists other evidence of thyroid inadequacy should be sought. It should, however, be borne in mind that perfectly developed eyebrows may be seen in individuals who have a high degree of thyroid insufficiency, and that in other instances the eyebrow may be deficient with a normal thyroid. This sign is of particular advantage in that it is easily observed.

Hamonic⁶ has studied the question of the relation of phimosis and incontinence of the urine, and he believes that a long adherent prepuce is a factor in causing it. He has performed 187 circumcisions for the exclusive purpose of curing this condition. Of these 130 were cured, 47 of which were relieved within from two to twenty-five days, and 83 after six weeks. Fifty-seven of the cases were lost sight of. In some instances there was a history of enuresis in the family. He believes that, both in boys and girls, genital irritation plays an important role in nocturnal incontinence.

The following table shows rather imperfectly the causes of nocturnal enuresis:

⁵ Bulletin de l'Académie de Médecine de Belgique, IV Series, tome xxi, No. 4.

⁶ Revue clinique d'Andrologie et de Gynécologie, 1909-10, p. 1.

Physiological	Taking too much fluid.
Eliminative	{ Due to faulty metabolism. { Eating too much salt, etc. { Due to drugs.
Urine	{ Hyperacidity. { Alkalinity. { Bacteriuria.
Genito-urinary organs	{ Inflammations { Urethritis. { Cystitis. { Pyelitis. { Malformations. { Calculi. { Tumors or polypi. { Hypertrophy.
Nervous system	{ Hypertonia or irritability of bladder. { Weakness of sphincter. { Reflex { Balanitis. { Vulvovaginitis. { Anal fissure. { Rectal polypi. { Intestinal parasites. { Malformation of spinal cord. { General irritability.
General	{ Diabetes mellitus. { Diabetes insipidus. { Rachitis. { Thyroid insufficiency. { Enlarged adenoids and tonsils.

IN a similar way the suggestions for treatment may be tabulated, but no pretence is made to include all of the things that have been suggested.

Restriction of fluids.	
Diet.	
Protection from cold.	
Rest and quiet life.	
Postural treatment.	
Waking child to empty bladder.	
Suggestion not to urinate.	
Suggestion to call out in sleep that there is a desire to urinate.	
Moral hygiene in lazy children.	
Reflex irritation	{ Passing catheter or sound. { Galvanic current. { Galvanic cautery. { Faradic current. { Injections of nitrate of silver solution. { Injections of normal salt solutions, etc. { Epidural injections (Cathelin). { Retrorectal (Jaboulay). { Perineal (Cahier).
Drugs	{ Atropine sulphate. { Strychnine sulphate. { Bromides. { Ergot. { Hexamethylenamine. { Desiccated thyroids.

Among the more interesting of the newer suggestions as to treatment are the results which have been obtained by Williams.⁷ He has published two series of cases which he has treated by the use of the desiccated thyroid. McCready has also written upon this subject. Williams' cases all belong to the class described above, and he obtained wonderfully satisfactory results in all except one case, and it is interesting to note that in this case the child did not have a subnormal temperature. Williams administered one-half grain of the dried thyroid twice daily to children who were between two and six years of age, and this amount may be increased somewhat for older children. The increase in dosage should be made slowly, as directly opposite effects are occasionally induced by overdosage. The results as described by Williams in his own words were exceedingly dramatic.

I have had occasion to use this method in a small series of cases, and these were not picked cases, as were evidently the cases in the series which Williams reports. In a small proportion of cases in which there were more or less marked signs that might be attributed to thyroid insufficiency, the results were quite remarkable. These were all children with adenoids and enlarged tonsils, or in some cases children in whom the adenoids and tonsils had been recently removed. In my series of cases the effect was obtained promptly or not at all. In every instance in which a favorable result was obtained a marked difference was noticed after the administration of one or two doses of the drug, and in all cases within a week.

Another remarkable observation which coincided with the result obtained by Williams, is that the undersized children gained weight rapidly. Williams mentioned one patient that gained five pounds in a week, and another, two pounds and seven ounces in a week. However, most of the patients gained less rapidly.

Another curious thing, which Williams has not mentioned, is that it has not been necessary to continue the thyroid over long periods of time, although in this regard I may have been accidentally fortunate and relapse in some cases may probably be looked for.

In several instances in which the children had high, arched palates but no subnormal temperature, the thyroids had no effect whatever.

Of the other methods of treatment with the newer remedies one may mention briefly the following:

Attention has been called to the use of hypnotism in the treatment of nocturnal enuresis by Voisin.⁸ He has reported one interesting case, in a boy, aged between thirteen and fourteen years.

⁷ Brit. Jour. Child. Dis., June, 1909. Lancet, 1909, i, 1245; Polyclin., London, 1909, xiii, 61.

⁸ Revue de l'Hypnotisme et de la Psychologie Physiologique, 1908-09, xxiii, 247.

In this patient the urine was sometimes passed without dreams, and at other times was accompanied by dreaming of the act. After several trials, Voisin was able to put the boy into hypnotic sleep, and on the following suggestion, that he would not dream any more, obtained a disappearance of the incontinence for six days. He was hypnotized again and the same suggestion made, which lasted for three days. He then made an epidural injection of artificial serum on three different occasions, and continued to hypnotize him once a week for a month. The patient has been entirely well for over a year. Voisin raises the question as to what the action of the epidural injection was in this case, whether the therapeutic effect was due to its action on the cauda equina, or whether it acted by suggestion. One is inclined to believe that the latter is the proper explanation. Among the rose-colored statistics are those of Culler, who treated 64 cases with hypnotism and claims to have cured 50 and bettered 10.

Genouville⁹ has made an interesting communication to the Association Française d'Urologie on a simple device which he has used with considerable success in certain cases. It probably acts as a sort of suggestion without words. He states that the idea of the apparatus is not original with him, but he has forgotten where he saw the mention of it. It consists of placing in the bed of the child under the region of the pelvis two metal plaques separated by a piece of flannel or a piece of absorbent cotton. These two metal plaques are connected with wires, each to one pole of a battery and a bell. When the infant urinates the cotton becomes wet, completes the circuit and causes the bell to ring. The infant is awakened and the micturition is stopped, and after being thus awakened several times, the patient is frequently cured. This has only been tried in a comparatively few cases by the inventor. A remarkable thing in connection with it is that most of the cases that were cured were cured very promptly. A modification of the device consists in having the apparatus arranged to give a slight electric shock on the abdomen of the child.

The use of the injection of salt solution has also been suggested. Cathelin has suggested making the injection directly into the spinal canal by means of lumbar puncture, or, in other instances, subcutaneously in the sacral region. Jaboulay has suggested retrorectal injections of 100 to 150 grams of salt solution, and Cahier¹⁰ has suggested subcutaneous injections into the perineum. He used between 60 and 70 grams, making the injections 1 or 2 cm. on either side of the median line. He claims to have had especially good results in the treatment of the adult cases.

Lozano and Forès¹¹ have used the epidural method with suc-

⁹ *Revue Prat. d. Mal. d. Org. gén.-urin.*, 1909-10, vi, 59.

¹⁰ *Arch. de med. et pharm. mil.*, 1909, liii, 401.

¹¹ *La Clinica Moderna*, April, 1911.

ness, injecting the solution into the spinal canal, making the injections low down in the sacral region toward the bottom of the canal. Whether the results obtained by these injection methods are purely to be attributed to the mental effect, or whether they act reflexly, one cannot say. In refractory cases this method might be tried.

Of the old-fashioned means of treating this disease there are one or two things which may be mentioned. The first is to place the child upon a simple non-irritating diet and to restrict the amount of fluid taken, particularly the amount of fluid taken after four or five in the afternoon. Secondly, in some cases raising the foot of the bed so that the irritable neck of the bladder is not quickly affected by the first urine which enters the bladder. Certain cases are improved by a large amount of rest and leading a quiet life. General reflex irritability may be caused by too strenuous a life, particularly long automobile rides and the like. I have seen on several occasions the simple directions to have the child stay in bed until it is ready to get up in the morning, and to lead a quiet life generally, result in cure.

In hospital practice a large proportion of the cases can be improved by a more or less dry diet and restriction of fluids. Where there is no other indication for treatment I have found the use of atropine to give better results in a greater number of cases than any other one thing in the suggestions made. To be of any service atropine must be given in full doses. In nocturnal cases a dose at five o'clock and at bedtime is all that is required. In cases occurring both during the day and night, the administration of the drug every three hours is to be advised. I usually prescribe a solution containing 1 grain of atropine sulphate in 2 ounces of water. Each drop of this represents approximately $\frac{1}{1000}$ of a grain, and ordinarily about as many drops will be required at a dose as the child is years old; but this is not the proper method of ascertaining the dose. Starting with one or two drops each dose should be increased one drop at a time until flushing of the face and neck occurs some twenty minutes after the administration of the drug. The dose should be diminished one drop, and this amount continued until the child has ceased urinating at night and for at least two weeks later, when the drug may be left off gradually, diminishing a drop at a time until one drop is reached, when it may be stopped.

It is hardly necessary to comment upon all the things mentioned in the table above. The chief object in writing this paper was to call attention to some of the things which have been published recently, and to call attention to the fact that there exists a small class of cases in which the thyroid insufficiency evidently causes nocturnal enuresis and which may be cured by the administration of the thyroid with great benefit to the general health and growth of the child.

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SOME APPLICATIONS OF THE CREHORE MICROGRAPH, WITH ESPECIAL REFERENCE TO THE RECORDING OF HEART SOUNDS.

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The purpose of this communication is to make a preliminary report of a few methods of using the Crehore micrograph¹ in the

¹ *Jour. Exper. Med.*, 1911, xiii, 616; *ibid.*, xiv, 339 to 365, and 520.

study of the physiology of the cardiovascular system in man and in animals.

Holowinsky² was the first to use the principle of light interference rings for the study of the function of the heart, but he used it only for the recording of heart sounds. His instrument is somewhat similar to the Crehore micrograph. He transmitted the sound vibrations electrically from a rather complex transmitter, placed on the chest wall, through an induction coil to an electromagnet actuating a diaphragm to which was attached a mirror in close apposition with a fixed glass plate, as in the Crehore micrograph. As a source of illumination he employed a magnesium light.

Crehore has constructed his instrument for taking two simultaneous photographic records, not, however, of heart sounds, but of the movements of the heart or pulse. He applies a suitable tambour to each of the two sites from which he desires to take tracings, for example, from the apex and from the radial. Each tambour is connected by rubber tubing with one of the interference instruments, which consists of a metal tambour the upper surface of which is formed by a thin brass diaphragm to the centre of which is fastened with colophonium a small mirror, while just above this mirror a glass lens is held stationary. The impulse from the apex beat or pulse is transmitted by the closed column of air through the tubing to the interference instrument where it produces movements of the metal diaphragm and, therefore, of the small mirror. The changes in distance separating the small mirror from the fixed lens above it cause the movements of the light interference rings produced by the rays from a mercury vapor lamp, these rings being photographed through a slit on a moving film.

In working with the Crehore micrograph we have found it necessary to make the following modifications and additions: (1) A time marker; (2) an electromagnetic signal; (3) a modification to permit the taking of more than two simultaneous pulse tracings; (4) an apparatus for taking tracings from the exposed mammalian heart; (5) an adaptation of the micrograph to the recording of heart sounds.

The methods we have used to meet these several deficiencies in the instrument are as follows:

1. *Time Marker.* Crehore estimates time intervals on the film by determining the average speed of the motor propelling the film, before taking each record, and calculating from this the number of inches per second of movement of the film. This method is, of course, accurate only when the film travels at a perfectly even rate, and this we have found not always to be the case. It was, therefore, considered advisable to introduce some more accu-

² Arch. d. physiol. norm. et patholog., 5 Sér., vii, 893; Zeitschr. f. klin. Med., 1901, xlii, 186.

rate form of time measurement. To accomplish this, a tuning fork, electrically activated, and set for twentieths of a second, was attached to the floor close to, but not touching, the micrograph. From its movable end a small cord was stretched to a fixed point on the opposite side of the micrograph in such a way that the cord extended just above, and close to, one of the interference instruments. The cord is placed so that it runs approximately perpendicular to the slit of the camera. When so arranged the vibrating cord causes a distinct sinuous shadow on the moving film, each complete wave representing one-twentieth of a second. This time curve is shown at the bottom of Fig. 1.

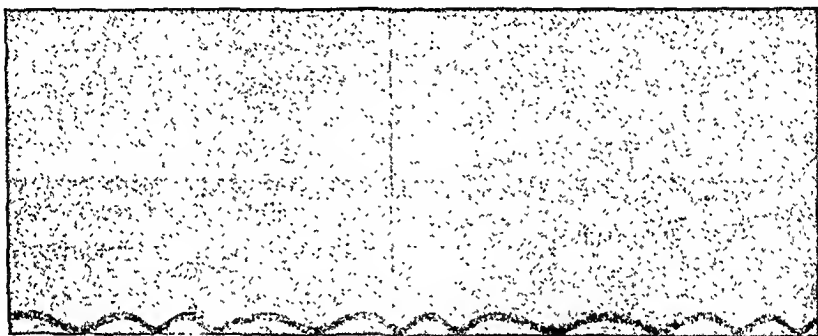


FIG. 1.—Record from right ventricle and jugular of dog. Time curve at bottom—
twentieths of a second.

2. *Signal.* The introduction of an electromagnetic signal was accomplished by placing the lever of such a signal just above, almost touching, one of the interference instruments so that its shadow also was thrown through the slit on to the film.

3. *Simultaneous Tracings.* The levers of Marey or other delicate tambours similarly placed permitted the recording of additional pulse tracings or of any other graphic tracings. We have thus taken, on one film five simultaneous tracings; the apex tracing on an interference instrument, the radial tracing on the other interference instrument, the carotid tracing with a Marey tambour, a time curve with the tuning fork, and the record of an electromagnetic signal. The ability to take simultaneous tracings from three or more sites has proved often of the greatest assistance in our studies.

4. *Tracing from Exposed Heart.* In taking tracings from the exposed heart it was found that the amplitude of the cardiac movement was so great that the impulse taken directly through a pneumatic tambour held against the heart had too great an amplitude for the sensitive interference instrument. Some method had, therefore, to be devised for reducing this amplitude without altering the character of the curve. It was also desired to localize the tracing to one part of the heart; a tambour held against the

heart gave the movements not only of that part of the heart, but also the changes in position of the heart as a whole. In order therefore, to reduce the amplitude of the pulsation and especially in order to localize the tracing to one part of the heart, we use a modification of the Cushny myocardiograph. This is shown in Fig. 2. It consists simply of the ordinary myocardiograph to which a tambour is attached that can be so placed that the upper end of the movable lever of the myocardiograph shall impinge constantly against the rubber dam, transmitting all its movements to the dam. By raising or lowering the fulcrum of this lever any desired amplitude of movement at its upper end may be secured. The tambour may be connected by tubing, either with one of the interference instruments, or with a Marey tambour, the lever of which is placed to throw its shadow onto the film. This instrument secures both the localization of the tracing to any particular part of the heart, and also the necessary reduction of the impulse amplitude, without, however, impeding the cardiac movement. For securing tracings from exposed vessels we use either a small funnel covered with rubber dam, to the centre of which a small piece of cork is attached, this cork being pressed gently against the isolated vessel, or we introduce a short glass cannula into the vessel, the cannula being filled with saturated magnesium sulphate solution and the end of the cannula away from the vessel being closed with rubber dam. Over this end of the cannula and the dam another rubber tube is drawn containing air, and this, in turn, connected with one of the interference instruments, transmits the movements of the dam to the latter.

5. *Recording of Heart Sounds.* For the recording of heart sounds we first considered the use of telephonic transmission, as in the Holowinsky instrument, but concluded that the record would be freer from adventitious waves if we could secure direct pneumatic transmission. This we have succeeded in doing by making the Crehore interference instrument more sensitive in the following way. One of the interference instruments was taken apart and its metal diaphragm removed. In its place the hard rubber diaphragm from a Bowles stethoscope, was substituted, this having been cut to fit the interference instrument. The small mirror was then attached to the centre of this hard rubber diaphragm with colophonium just as it had been attached to the metal diaphragm. The stationary lens was replaced and the adjustment of the rings conducted in the usual manner. The interference instrument thus produced is at least five times as sensitive as the original instrument, and when properly connected with the heart brings out very distinctly the sound vibrations produced by the heart. It is not, however, so sensitive as to be disturbed by the ordinary vibrations of the room. The method of connecting it with the chest is as follows: The instrument is

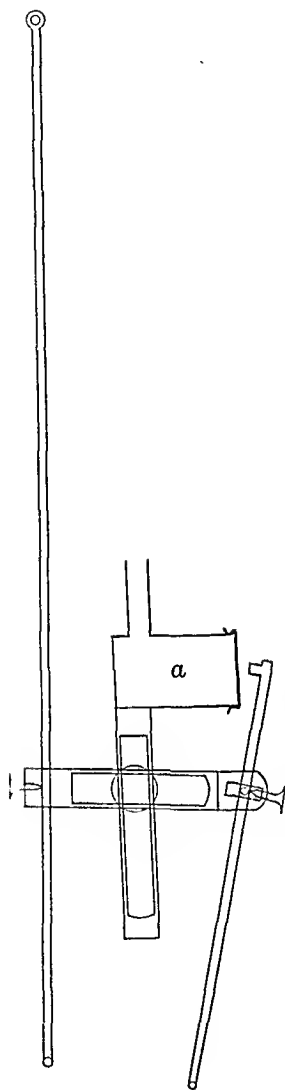


FIG. 2.—Modified Cushny myocardiograph (reduced one-half). *a*, tambour.

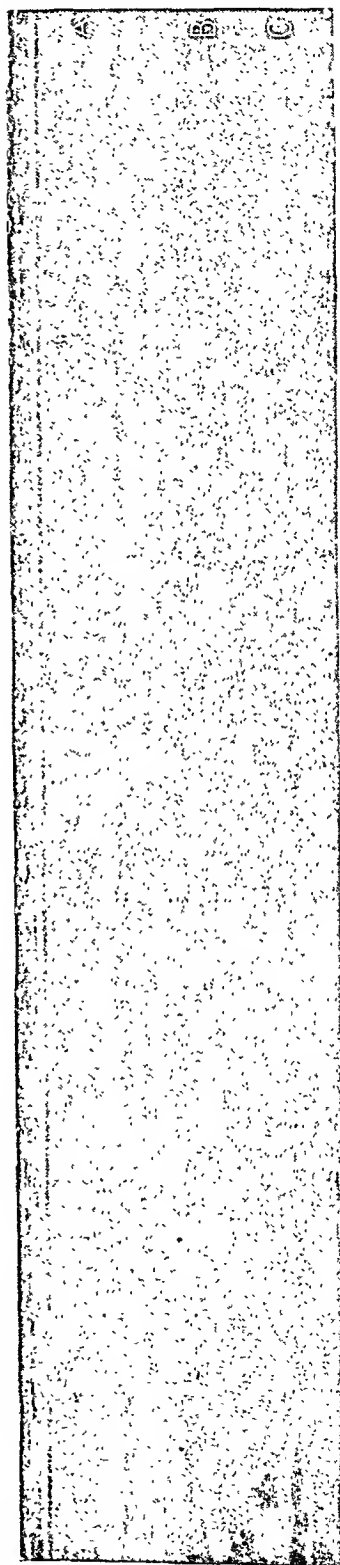


FIG. 3.—Photographic record of normal human heart sounds (*A*) apex tracing (*B*), and time curve (*C*). Tracing represents one cycle.

connected by thick-walled rubber tubing of 3 mm. inside diameter with the chest piece of a Bowles stethoscope. In the course of the tubing one of the air valves belonging to the micrograph is placed. When the chest piece of the stethoscope is applied to the precordium and this air valve left slightly open, the gross shock of the apex beat is not transmitted, while the more rapid vibrations causing the sounds are well transmitted to the interference instrument. The accompanying photograph (Fig. 3), shows such a record, with a simultaneous record of the apex beat recorded from the other unmodified interference instrument by Crehore's method (Fig. 4).

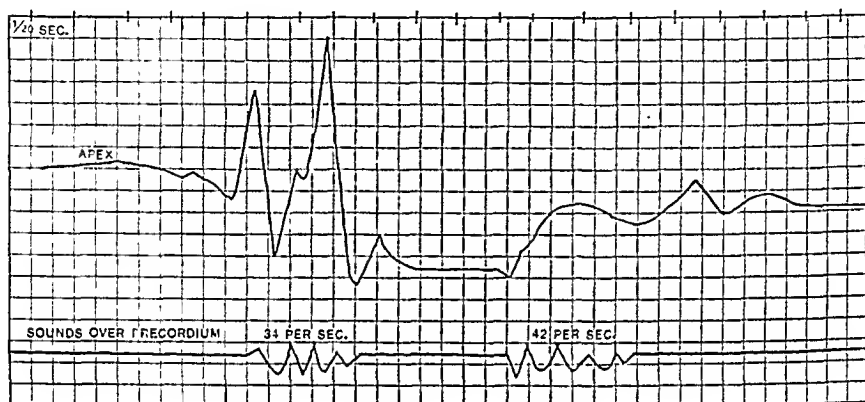


FIG. 4.—Curve plotted from Fig. 3.

Incidentally, it may be mentioned that a mirror fastened at an angle of 45 degrees above the ground glass of the micrograph, enabling the operator while on the floor adjusting the rings to watch, by reflection, the ground glass image of the rings, is a small addition of great service.

These applications to the Crehore micrograph of various forms of physiological apparatus have been found of value in the study of various problems concerning the physiology of the heart and circulation; the results of these studies will be presented in a later communication.

SARCOMA OF THE TONGUE AND CONDITIONS WHICH SIMULATE IT.

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PRIMARY sarcoma of the tongue is a lesion peculiar not only for its rarity but on account of the difficulty in diagnosis in many cases. When the tumor is pedunculated the various forms of

chronic inflammation need not be considered; still, the differential diagnosis between sarcoma and granulation tissue may present some difficulty. If the sarcoma is of a diffuse form the difficulties in distinguishing it from the lesions of syphilis, tuberculosis, macroglossia, and chronic glossitis are so great that both clinically and pathologically various observers may often express a different opinion. Under these circumstances it has seemed justifiable to report in connection with cases of sarcoma of the tongue a diffuse enlargement of part of the tongue which may have been sarcoma, although the bulk of the evidence, both clinical and microscopic, is rather against this diagnosis. There are many points of similarity between this case and some of the others reported as sarcoma by different writers which make it seem probable that a more exhaustive study of their cases might have altered the diagnosis of sarcoma; for example, in Cases XXIV and XLVI.

The patient whose malady led to the study of this subject first consulted me at the New York Skin and Cancer Hospital, July 14, 1910. He was then aged forty-five years, of previous good health, married, and the father of two healthy children. He had always led a temperate life, and his first serious illness was a rectal abscess in January, 1901. This was incised and drained, but did not heal. It was three times operated upon in the succeeding three years, and so far healed that in the last five years it had occasioned the patient no other difficulty than a slight mucous discharge. A proctoscopic examination made by Dr. Mayo, in June, 1910, showed no lesion of the mucous membrane, but an indurated rectum with a tendency to stricture formation.

About 1906 the patient's mouth became tender, the lips, cheeks, roof of the mouth, and gums swelling. In December, 1909, portions of the lips and cheeks were cut away, and in July, 1910, the tongue was twice cauterized.

Although the patient gave no syphilitic history and had never had early symptoms of syphilis, his disease had more than once been diagnosticated as of this character, and three times he was given a thorough course of antisyphilitic remedies without any beneficial result. Local applications were equally inefficient.

When the tongue was examined it was seen to be moderately swollen, especially the anterior half on the left side. Back of this on the left margin of the tongue was a scar from previous cauterization, the edges of which were somewhat swollen and tender. There were no irregularities of the teeth which might irritate the tongue. The lips showed scars of previous operations and were somewhat inelastic.

Under cocaine, November 9, 1910, assisted by Dr. Bainbridge, the scar was excised and a large wedge-shaped piece was removed from the dorsum of the tongue, on the left side, both wounds being sutured. Primary union resulted.

Examination of the blood at this time showed 5,000,000 red cells and 9000 white; the differential count being polynuclears, 57.2 per cent.; lymphocytes, 37 per cent.; eosinophiles, 3.4 per cent.; and transitionals, 2.4 per cent.



FIG. 1.—Tumor of the tongue simulating sarcoma.



FIG. 2.—Tumor of the tongue simulating sarcoma.

December 9, 1910, a Wassermann test was made with a negative result and the blood was carefully searched for spirochetæ, but none were found.

The tongue continued to increase in size, and changes previously

existing only on the left side spread to the right, so that at the time the photographs (Figs. 1 and 2) were taken, approximately the anterior third of the tongue was involved, the lesion extending farther back on the left than the right. The mucous membrane was unbroken. The affected anterior part of the tongue was slightly darker and slightly denser than the normal posterior part, the line between the two being fairly definite. The affected portion was elevated one-third of an inch or more above the normal portion. Indentations caused by pressure of the teeth are plainly shown in the photographs. Later, shallow pressure ulcers developed in these indentations and the tongue increased so in size that it was retained in the mouth with some difficulty. There was a constant drooling of saliva. The mucous membrane of the hard palate now showed alteration, in places being thicker than normal and thrown into unnaturally deep folds. The lymphatic glands under both sides of the lower jaw were enlarged.

Dr. Coley, who saw the patient in consultation, considered the disease macroglossia of the chronic inflammatory type.

On January 26, 1911, I amputated about one inch of the tongue, extending the excision farther back in the central portion so that the wound could be sutured. It healed primarily.

Four pathologists who examined the excised portions gave the following reports:

Dr. Ewing: "Macroglossia from chronic myositis and secondary plasma-cell infiltration of the tissue."

Dr. Fordyce: "The condition may be a sarcoma, but I should hardly feel inclined to commit myself definitely to this diagnosis."

Dr. Jessup: "It seems possible to rule out carcinoma, sarcoma, and syphilis, and in the absence of giant cells, tubercle tissue, and bacilli there is slight ground for the diagnosis of tuberculosis. The cells of the growth have the appearance of plasma cells, and pathologists who have seen the sections say that the appearance resembles that seen in cases they had considered tuberculous. For lack of a better name the term plasmona might be employed."

Dr. Jeffries: "A small, round-celled sarcoma."

The accompanying microphotographs (Figs. 3 and 4) show very clearly the type of microscopic picture obtained with the high and low power lenses. They were essentially the same in all portions of the diseased tongue.

In February and March, 1911, the patient had fourteen injections of the mixed toxins of prodigiosus and erysipelas. At first, these seemed to check the growth, but later this continued and the injections were abandoned. In April, 1911, the patient was given a full dose of salvarsan without benefit.

Injections of pyoktanin, which had proved so satisfactory in Case XXIV, reported below, were next employed. In that case a preliminary tracheotomy was performed as a safeguard against

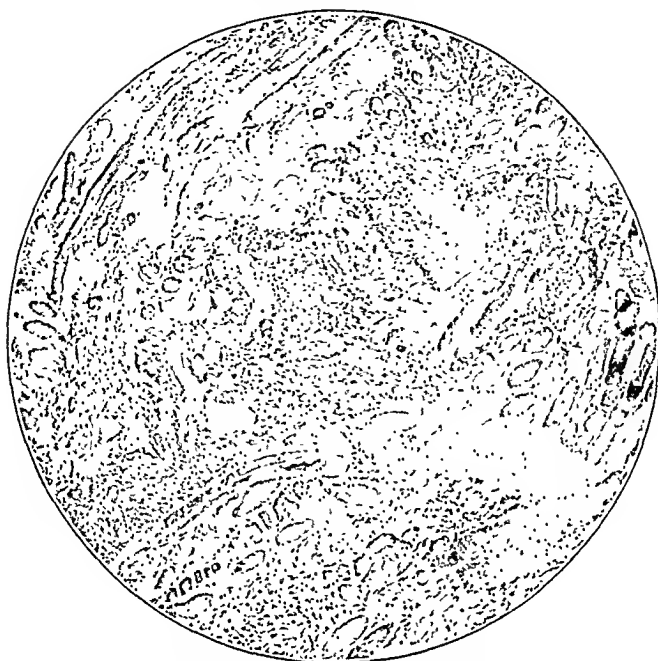


FIG. 3.—Microphotograph made under Dr. Ewing's direction, showing appearance of specimen under the low power. The separation of the bands of muscle fiber is plainly shown.

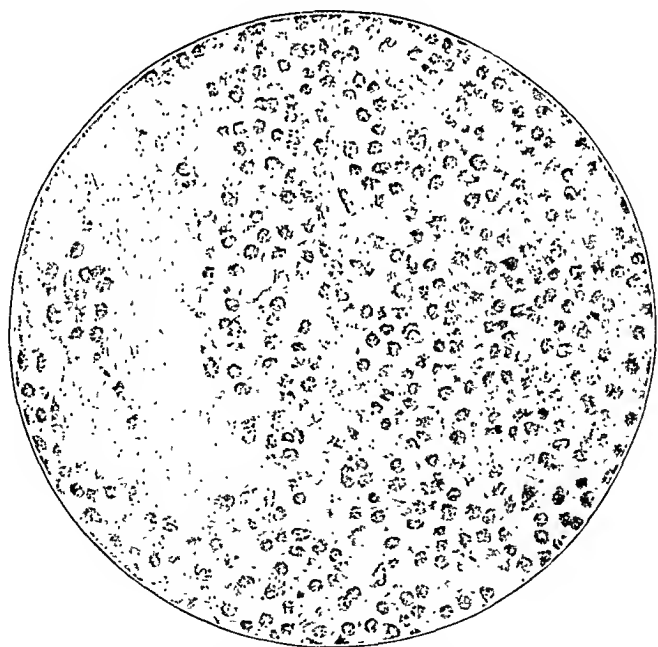


FIG. 4.—Section of tongue shown under high power. Photograph from preparation made by Dr. Jessup, showing the plasma cells and the broad band of degenerated muscle fiber.

possible sudden swelling of the tongue following the injections. The anticipated swelling did not occur. As the swelling in my patient's tongue had not yet reached its posterior part, it seemed perfectly safe to begin with small amounts of pyoktanin without a preliminary tracheotomy. By the time he had received three injections the swelling of the tongue was so much increased that they were abandoned. Thus far, nothing but operations had given any relief. The tongue continued to swell, and on May 19, 1911, in company with Dr. Gerster, I again amputated the anterior portion of the tongue; this time so far back that the remainder of the organ when at rest did not extend forward beyond the molar teeth, although it could be pushed forward nearly to the incisors. The resulting wounds healed chiefly by granulation. When healing was complete and the tongue had shaped itself to the floor of the mouth, it reached, when at rest, to the base of the incisor teeth. In the succeeding months it showed no tendency to increase in size except on the right margin just in front of the tonsil. This superfluous tissue was cut away under cocaine, and that part has since remained quiet. Following this operation, the swelling of the lymph glands under the jaw disappeared.

In August, 1911, the patient developed a cough. An examination of the sputum showed it to contain tubercle bacilli. In spite of anything I could say, the patient refused to apply to any physician for suitable treatment nor would he furnish sputum for another microscopic test. When last heard from, November 8, 1911, he still insisted that his trouble was not tuberculous, although his cough had not left him. The tongue was a little tender, but showed no return of the long-standing disease.

When we turn to medical literature to review what has been written upon sarcoma of the tongue, we find reports of nearly 50 cases. From the data given it is well nigh impossible to make any satisfactory classification in these cases. Some previous writers have attempted to divide them into cases of true sarcoma and those of the doubtful character. Such a classification would be instructive if it was reliable; but neither the histories nor the clinical appearances, nor the pathological reports, nor statements as to the outcome, are sufficiently full or uniform to warrant such a classification. It seems better therefore, merely to number the cases chronologically, giving the reference of each, for the sake of those who wish to further investigate the subject.

The tumor was said to be pedicled in 7 of the 48 recorded cases. In a few other cases it is spoken of as globular, but this might or might not imply the existence of a distinct pedicle. In some cases the tumor is described as distinctly firmer than the rest of the tongue. In others, it is stated that, even when ulceration was present, it was as soft as the normal tongue.

The descriptions of the gross appearances of these tumors show

clearly how ridiculous it is to describe such things by comparing them with objects in nature. Those who do this usually make the mistake of comparing a growth to an object much larger than it really is. Thus when one speaks of a tumor "as large as an orange" existing in the dorsum of the tongue, inaccuracy is evident, for the mouth will not contain even a very small orange. Another writer speaks of removing two tumors, one as large as a hen's egg and the other as large as a walnut. This, again, is a physical impossibility. "As large as a nut" may mean anything from a beech nut to a cocoanut, and the very indefiniteness of the comparison destroys its value. A "bean" is another vegetable product which varies greatly in size. A "fives ball" is a near relative of the well-known tennis ball, but it must be a very much shrunken relative to find accommodation in the left side of the tongue. With two good standards of measurement at our disposal, viz., inches and centimeters, it is unfortunate that such inaccuracies of description should be found in scientific reports.

Ulceration is not an early or common symptom. It is mentioned in only 11 cases, and in 3 of these the ulcers were shallow and apparently due to pressure against the teeth when the mouth was overfull. Such ulcers occurred in my patient, but speedily healed when operation reduced the bulk of the tongue and removed pressure. The excavating hard ulcer so characteristic of carcinoma is rare in sarcoma of the tongue. The cases in which it occurred are Case IV, probably a carcinoma; Cases IX and XLVIII, lymphosarcomata; Case XI, in which the ulcer followed incision into a cyst containing calcareous matter. In Cases XIX and XLVII ulcers were present apparently without induration, and the tumors were respectively round-celled and spindle-celled sarcoma. In 16 cases, ulceration or its absence is not mentioned. From the description of the operation in some of these cases ulceration was surely absent; but granting its presence in some of the others, it must still be classed as a very rare symptom of sarcoma except as a result of traumatism, such as incision or constant pressure against the teeth when the tumor has overfilled the mouth.

Another point of importance in diagnosis is the presence of enlarged glands. Such glands are mentioned at the time of the first operation in 13 cases. Their absence is noted in 15 cases. In 9 cases they appeared subsequent to the first operation, although in 4 of these cases there were no glands present at the time of the first operation.

There were some striking recoveries with freedom from recurrence for long periods of time. Recurrences with the death of the patient are mentioned in 6 cases, but in 3 others extensive post-operative recurrences were present at the time of the report. In 21 cases no recurrence was present at the time of the report, although

in some of these the period that elapsed between the last operation and the report was only a few months. There were also some striking recoveries after extensive involvement either of the tongue or of tongue and lymph glands as well. For example, in Case XVIII a spindle-celled sarcoma involved the right half of the tongue beyond the median line; there were no glands at the first operation; the tumor recurred locally, and involved the left sub-maxillary lymph glands, necessitating the second operation. Still further recurrence was removed by a third operation, thirteen months after the first, and two years later there was no sign of recurrence. In Case XXI, there is no mention of glands being involved. An extensive removal of the tongue and floor of the mouth was twice performed, with an interval of nineteen months between operations. A year after the second operation there was no recurrence. In Cases X and XLI glands were involved and were removed at the first operation. There was no sign of recurrence for periods varying from eight months to several years. Case XLVIII presents a still more remarkable record in that glands were present and removed at the time of the first operation. At a later operation other glands showing metastases were removed, and five years after the second operation the patient was free from recurrence. In Case XXX, removal of part of the tongue and involved lymph glands was three times performed at intervals of one month each. Following the last operation, recurrence again developed, grew for a month, and then without further operation this disappeared, leaving no trace in seven months. In Case XLIV, there were no glands present at the time of the first operation. The patient died eleven months later and was found to have extensive involvement of the abdomen, looked upon as metastases from the primary tumor of the tongue.

From the character of these reports it is impossible to draw satisfactory conclusions as to the mortality following operation or the probability of recurrence.

CASE I.—Fiedler.¹ Male, aged forty years, a teacher. For eighteen years he suffered from hoarseness, especially in winter; for six years from a cough, and for two months from difficulty in swallowing. A broad tumor at base of tongue was just visible when mouth was wide open. Portions of tumor, one "as large as a hen's egg" and another "as large as a walnut" were removed with the galvanocautery. Spindle-celled sarcoma.

Rapid local recurrence with involvement of the tonsils and cervical lymph glands. Two months after first operation masses weighing $1\frac{1}{4}$ ounces removed with galvanocautery. Patient died two months later after almost choking for some days. Mass measured 7 cm. across, 8 cm. lengthwise, and 2 cm. high.

¹ Zeitschr. f. Med. Chir. u. Geburts., 1864, n. f. iii, p. 305

CASE II.—Lücke.² Male, aged thirty-six years, had a tumor slowly growing for seven years, the size of a walnut. The tumor was shelled out of a distinct capsule. Examination showed oval and round cells, many hyaline degenerated; centre of tumor calcified; considered a cholesteatoma. No recurrence.

CASE III.—Jacobi.³ Male, aged three months, had a congenital, rapidly growing tumor on dorsum of tongue; not pedicled; size of walnut. No ulcer. No enlarged glands. Excision by galvanocautery. Spindle-celled sarcoma. Two weeks later wound granulating.

CASE IV.—Heath.⁴ Male, aged sixty years, suffered for six months with a painful ulcerating tumor of under surface of tongue. Sharply circumscribed more to the left than the right and involving the floor of the mouth. One enlarged gland beneath the jaw. Excision of tumor after division of jaw. "Medullary cancer." (Cited by Marion and others as a round-celled sarcoma.) No recurrence in eight months. The swelling in the lymph gland had disappeared.

CASE V.—Hueter.⁵ Female, adult, noticed at fifth month of pregnancy a swelling of the dorsum of the tongue, which grew rapidly; two months later it was the size of a hazel nut. Excision of tumor. Sarcoma. Subsequent history not given.

CASE VI.—Albert.⁶ Female, aged fifty-six years. For one year she had pain on swallowing; for some months a tumor widely attached to base of tongue obscured the pharynx. It was sharply differentiated from the substance of the tongue. Excision of tongue and tumor close to hyoid bone. Round-celled sarcoma. Death from pneumonia in eight days.

CASE VII.—Hutchinson.⁷ Male, aged twenty-two years, had a painless growth for twelve years or more, which finally filled the mouth and embarrassed speech, breathing, and swallowing. No ulceration or enlarged glands. Removal after division of symphysis of jaw and tracheotomy. Sarcoma or lymphosarcoma. Weight, 7 ounces. Good health for two years, then rapid recurrence in scar and death.

CASE VIII.—Santesson⁸ (Operator, Berg). Male, aged thirty-one years, had a swelling in tongue three years, chiefly in right half. Severe hemorrhages from several small ulcers. Enlarged lymph glands had existed for fifteen years, possibly scrofulous. Palpation showed a hard tumor covered by thinned mucous membrane. Tracheotomy; excision of lymph glands of right side; ligation of right lingual; excision of tongue. Plexiform sarcoma with hyaline degeneration. Death in seven days from sepsis.

² *Jahr. v. Virchow-Hirsch*, 1866, i, 173.

⁴ *Trans. Path. Soc., London*, 1869, xx, 157.

⁶ *Wien. med. Presse*, 1885, p. 171.

⁸ *Nord. med. Arkiv.*, 1887, vol. xix, No. 18, p. 1, and *Zentralbl. f. Chir.*, 1889, p. 506.

³ *Amer. Jour. Obstet.*, 1869, ii, 81.

⁵ *Berl. klin. Woch.*, 1869, p. 346.

⁷ *Lancet*, 1885, i, 1084.

CASE IX.—Beregszaszy.⁹ Male, aged forty-two years. For two months he noticed a growth at base of the tongue, with pain and ulcer; also glandular enlargement. No treatment. Death in eight days from metastasis in peritoneum. Growth in tongue considered the original lesion. Pathological report, lympho-sarcoma.

CASE X.—Butlin.¹⁰ Male, aged forty years, a smoker; free from syphilis; for two months had a tumor of the left side of the tongue the size of a "fives ball." No ulcer. Hard submaxillary gland. Left half of tongue and glands removed. Small round-celled sarcoma. No recurrence in several years.

CASE XI.—Godlee.¹¹ Female, aged twenty-four years; noticed for five weeks sore spots on under surface of tongue near the tip, developing into a tumor. It was diagnosticated as abscess and punctured. It contained calcareous matter, and wound was drained. In a few weeks ulcer was excised. Prompt recovery. Adenosarcoma. Cysts, some of them filled with calcareous material, were surrounded by tissue thought to be sarcomatous, composed of round and spindle cells. Subsequent history not given.

CASE XII.—Mandillon.¹² Female, aged twenty years. From this patient a tumor the size of a pea near the frenum of the tongue was removed with the thermocautery. It recurred in three months, and was excised and the wound cauterized. No microscopic examination. Considered sarcoma. Second recurrence in a few months locally, but larger than before.

CASE XIII.—Bleything.¹³ In a male, aged seventeen years, cigarette smoking and a broken tooth were thought to have caused a painful elevated nodule on right border of tongue near the tip with an indurated base. No enlarged glands. Excision and cauterization failed to effect a cure. Later, excision of a triangular portion of tongue containing the lesion. Round-celled sarcoma, or possibly granulation tissue. No recurrence in six years.

CASE XIV.—Mercier¹⁴ (Operator, Mercanton). Male, aged thirty-six years, had for eight years a pedicled tumor, the size of a nut, on the dorsum of the tongue in median line, growing slowly, without pain. No ulceration. No enlarged glands. Tumor excised with a portion of the tongue at its base. Wound sutured. Primary union. Sarcoma with giant cells. Fatty degeneration in the centre of the tumor. Subsequent history not given.

CASE XV.—Targett¹⁵ (Operator, Durham). In a male, aged two years, a tumor was noticed for seven weeks rapidly growing

⁹ *Krankheiten d. Zunge von Butlin*, 1887, p. 226.

¹⁰ *Lancet*, 1887, i, 623, and *Diseases of the Tongue*, 1900, p. 301.

¹¹ *Trans. Path. Soc., London*, 1887, xxxviii, 346.

¹² *Jour. de Méd. de Bordeaux*, 1888, xviii, p. 189.

¹³ *New York Med. Jour.*, 1888, xlvii, 683.

¹⁴ *Rev. Méd. de la Suisse rom.*, 1890, p. 250.

¹⁵ *Guy's Hosp. Rep.*, 1890, p. 24.

without pain. Tumor one inch in diameter of dorsum of tongue; one and one-half inches behind tip. No ulcer. No enlarged glands. Observation for two months, then removal with ecraseur. Rapid local recurrence so that in a fortnight it was larger than before operation. Mixed celled sarcoma. Death in a few weeks.

CASE XVI.—Targett¹⁶ (Operator, Howse). A male, aged sixty-five years, noticed for one year a painless, globular swelling most prominent on under surface of tongue and deeply connected with a similar swelling in the floor of the mouth on the left side. No ulcer. Enlarged gland below the jaw. Anterior two-thirds of left half of tongue removed, together with mass in floor of mouth. Round-celled sarcoma. Fifteen months later large recurrence in left side of neck and another in the right cheek. No recurrence in mouth. Two years after operation, patient still in poor health, tumor masses constantly growing; mouth still free.

CASE XVII.—Mikulicz.¹⁷ Female, aged twenty-four years, noticed for three months a small nodule on dorsum of tongue growing without pain. Bleeding only when injured by teeth. Pedicled nodular tumor, 1.5 cm. in diameter, about 1 cm. from tip of tongue. Pedicle one-third the diameter of tumor. Excision of tumor with thermocautery, the cut being made through the base of the pedicle. Sarcoma. Subsequent history not given.

CASE XVIII.—Mikulicz.¹⁸ Male, aged fifty-seven years, had for six months a gradually increasing swelling of right half of tongue reaching beyond the median line. No pain nor ulcer. No enlarged glands. Removal of tongue to a point back of the disease. Spindle-celled sarcoma. Local recurrence and involvement of left submaxillary lymph gland required other operations seven and thirteen months after the first. Two years after the third operation there was no sign of recurrence.

CASE XIX.—Scheier¹⁹ (Operator, Körte). Male, aged twenty-eight years, suffered for six months pain and swelling of tongue; followed by deep ulceration well back on the dorsum behind circumvallate papillæ. Antisyphilitic remedies without effect. Growth soft in spite of deep ulceration. One enlarged gland. Preliminary tracheotomy: Division of lower jaw back of first molar; removal of tumor and most of base of tongue; cauterization of surface of wound; suture of divided jaw. Small round-celled sarcoma. Rapid recurrence filling the floor of the mouth in six weeks and only partly overcome by a second operation. Death in eleven months from enormous growths of both sides of neck.

¹⁶ Guy's Hosp. Rep., 1890, p. 21.

¹⁷ Mikulicz und Michelson, Atlas d. Krankheiten d. Mund u. Rachenhöhle, 1892, No. 2, Pl. 35.

¹⁸ Ibid., 1892, No. 3, Pl. 37.

¹⁹ Berl. klin. Woch., 1892, p. 584.

CASE XX.—Stern.²⁰ Female, aged four years, an idiot; had a tumor of right margin of tongue, well back, the size of a filbert. Excision of tumor. Spindle-celled sarcoma. Recurrence locally in seventeen months, led to second excision of tumor with wider margin of tongue. Subsequent history not given.

CASE XXI.—Schulten.²¹ Female, aged thirty-two years, had difficulty in swallowing for five months on account of a tumor at base of tongue almost filling throat. Tonsils and epiglottis not involved. Growth projected below chin. Tracheotomy; ligation of both linguals; pharyngotomy; extirpation of root of tongue and tumor. Weight, 92 grams. Sarcoma. Nineteen months later extensive recurrence in floor of mouth and remains of tongue. Tracheotomy; extensive removal of tumor and tongue. Complete healing in four months. Patient well a year after second operation.

CASE XXII.—Onodi.²² Female, aged seventeen years, for six months noticed a tumor as large as a bean at the right side of the base of the tongue. It grew without pain to the size of a small nut, still covered by normal mucous membrane. Section removed for examination. Fibrosarcoma. Removal of tumor proposed and refused. One month later condition about the same. Ulcer caused by the removal of section was still unhealed.

CASE XXIII.—McBurney.²³ Male, aged thirty-six years, had had several applications of the galvano-cautery for discomfort in the throat. From a tumor over two inches by one inch, which occupied the back of right half of tongue, a section was removed and proved sarcomatous. Preliminary tracheotomy. Through incision below the jaw the right half of the tongue, right half of epiglottis, a part of the right wall of the pharynx, and right tonsil were excised. Wound partly sutured. Good recovery. Swallowing perfect. In three months recurrence in the submaxillary region was widely excised and skin grafted. Two years later no further recurrence.

CASE XXIV.—Perman.²⁴ Female, aged thirty years, had for six months an unpleasant feeling in the throat, with occasional streaks of blood. Examination revealed a tumor at base of tongue about 1.5 to 2 cm. in diameter. No ulceration. Density about the same as the rest of the tongue. Iodide of potash given without result. Section removed for examination proved to be sarcoma. Removal of tongue refused. Preliminary tracheotomy and pyoktanin injections, 1 or 2 grams of a 1 to 500 solution, every other day. No swelling of tongue. Tumor much reduced by five injections; disappeared after thirty-one injections and two applications of the galvanocautery. Ten months later no recurrence.

CASE XXV.—Abbe.²⁵ Male, aged seventeen years, for some months noticed a mass in dorsum of tongue about one inch in

²⁰ Deut. med. Woeh., 1892, p. 495.

²¹ Deut. Zeit. f. Chir., 1893, xxxv, 417.

²² Rev. de Laryngol., etc., 1893, p. 886.

²³ Med. Rec., 1893, xliii, 439.

²⁴ Hygiea (Stockholm), 1894, p. 367, and Buffalo Med. and Surg. Jour., xxxiv, 148.

²⁵ Annals of Surgery, 1894, xx, 72.

diameter. No ulcer. Removal of tumor with capsule, suture of wound. Angiosarcoma (Hartley); pure sarcoma (Eliot and Ferguson). No recurrence in nine years.

CASE XXVI.—Dunham²⁶ (Operator, Bryant). In a male, aged sixty-one years, a bite of the tongue was followed in eight months by formation of a tumor in the right margin about one inch from tip; globular; discrete; about one inch in diameter. No ulcer. Excision of tumor. Sarcoma, composed mostly of large round cells. Subsequent history not given.

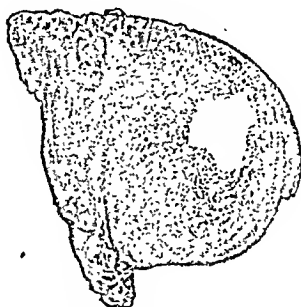


FIG. 5.—Sarcoma of tongue. (Dunham.)

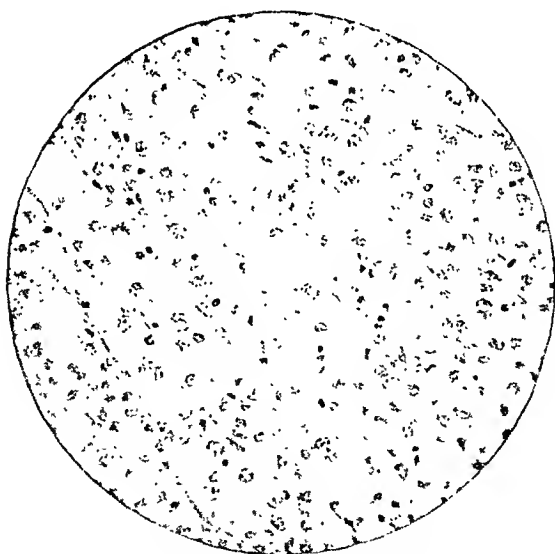


FIG. 6.—Photomicrograph of sarcoma of tongue composed mostly of large round cells. (Dunham.)

CASE XXVII.—Murray.²⁷ A woman aged fifty-six years. History of removal of a cyst under tongue five years previous and a small hard tumor from floor of mouth five months previous. Examination showed a firm tumor of right side of floor of mouth

²⁶ AMER. JOUR. MED. SCI., 1895, cx, 259.

²⁷ Annals of Surgery, 1895, xxii, 271.

and tongue with enlarged glands beneath jaw. No ulceration. Whole tongue and mass beneath removed in one piece after tracheotomy. Round the spindle celled sarcoma. One year later no recurrence. This tumor probably started in the floor of the mouth.

CASE XXVIII.—Perkins.²⁸ Male, aged twenty-six years, had a tumor of dorsum of tongue growing since four years of age, but the last year rapidly. No pain. No ulcer. No enlarged glands. Excision three-quarters tongue. "A slow malignant tumor consisting principally of small round cells, among which are a number of isolated connective tissue fibers" (McFarland). Twenty months later recurrence in floor of mouth and small glands in both submaxillary regions. Further operation refused. Outcome not known.

CASE XXIX.—Marion²⁹ (Operator, Poncet). In a male, aged thirty-two years, with no apparent cause, the left half of tongue swelled so suddenly as to embarrass swallowing, speech, and respiration. An incision evacuated foul pus, the swelling partly subsided, and the wound healed, leaving the left half of the tongue larger than the right. It grew slowly for six years, then more rapidly for two years, until speech and swallowing were again difficult. Examination showed a large mass beneath the tongue pushing downward so as to appear above the hyoid right and left. No ulcers. No enlarged glands.

After division of the inferior maxilla in the median line the tumor was removed from its capsule with some parts of the mucous membrane, but little of the muscle of the tongue. Sarcoma with much elastic tissue. Weight, 400 grams. Four years later, no recurrence.

CASE XXX.—Marion³⁰ (Operator, Berger). Male, aged seventeen years, stated that for six months the left side of the tongue was often bitten. For two months he had noticed a slowly growing tumor. A tumor the size of a small nut in the left border of the tongue, 3 cm. from the tip, pedicled, and having shallow ulcerations. Small glands in each submaxillary region. Section removed and pronounced spindle-celled sarcoma. Tumor excised with wide margin of healthy tissue. One month later local recurrence. Glands larger than before. Removal of glands both sides of neck and partial excision of tongue; after ligation of the left lingual artery. One month later local recurrence. Division of the inferior maxilla and removal of left half of tongue. One month later local recurrence, which grew rapidly for one month, then slowly disappeared. In seven months no trace remained.

²⁸ Ann. Surg., 1896, xxiii, 585.

²⁹ Rev. de Chir., 1897, xvii, 682.

³⁰ Ibid., 1897, xvii, 677.

CASE XXXI.—Liehtwitz.³¹ Female, aged twenty-five years, noticed for six weeks a pedieled tumor size of "nut" on dorsum of tongue 2 cm. from the tip and slightly to the left of the median line. No ulcer. Excision of tumor with its base by electrocautery. Tumor, 9 mm. in diameter, is an angiosarcoma. Two years later, no recurrence.

CASE XXXII.—Littlewood.³² Male, aged seventeen years, scalded his tongue. Ulcer never healed. Mercury and potassium iodide three months without benefit. Two years later centre of tongue had enlarged to size of "orange." Two small ulcerations. Excision of tongue and three weeks later of glands on both sides of neck. Round-celled sarcoma—infiltrating. Growths appeared subsequently in left tonsil, both sides of neck, and right temporal muscle. Death in five months.

CASE XXXIII.—Delbaneo.³³ (Operator, M. Schmidt). An infant, aged fourteen days, presented a diffuse congenital tumor of the left border of the tongue in its anterior part. Excision of tumor. Diffuse sarcoma, chiefly spindle celled. Secondary degeneration of muscle fibers. Result not given.

CASE XXXIV.—Melchior-Robert.³⁴ (Operator, Villeneuve). Female, aged sixty-four years, suffered for three months pain in right side of tongue especially on swallowing. Had bad teeth extracted, and later noticed a spherical tumor the size of large nut attached by a pedicle to right side of tongue 3 or 4 cm. ($1\frac{1}{2}$ inches) from its tip. Superficial ulcerations were present. Tumor excised with V-shaped piece of tongue. Wound cauterized and sutured. Six days later a profuse hemorrhage; then wound healed. Round- and spindle-celled sarcoma. No sign of recurrence two and one-half years later.

CASE XXXV.—Downie.³⁵ (Operator, MacEwen). Male, aged twenty-three years, thought a fishbone became fixed in the back of the tongue. Discomfort for four months, with difficulty in swallowing and loss of weight. Repeated examinations failed to show any foreign body. The right half of the tongue was swollen chiefly toward its base, also the right tonsil. Shallow pressure ulcers from teeth. Section removed for examination. The whole tongue and neighboring structures removed. Round-celled sarcoma. Result not given.

CASE XXXVI.—Downie.³⁶ In a male, aged thirty-four years, without apparent cause, there was bleeding from the mouth for several weeks with rapid loss of weight. There was then noticed a pedunculated tumor, size of a walnut, springing from the left side of the base of the tongue behind the circumvallate papillæ.

³¹ Gaz. heb. des Sci. Méd., 1898, xix, 199.

³² Münch. med. Woch., 1898, xlv, 155.

³³ Brit. Med. Jour., 1899, ii, 1065.

³⁴ Lancet, 1898, i, 507.

³⁵ Rev. de Chir., 1899, xvii, 546.

³⁶ Brit. Med. Jour., 1899, ii, 1065.

Tumor excised after division of the left cheek back to the masseter muscle. Wounds healed primarily. Spindle-celled sarcoma, weighing 28 grams (about one ounce). Patient rapidly recovered normal weight. Four months after operation no sign of recurrence.

CASE XXXVII.—Butlin³⁷ (Operator, Barling). In a female, aged thirty-five years, there developed in four months an elastic swelling limited to left half of tongue, noticeable on both upper and under surfaces. No ulcer. No enlarged glands. Left half of tongue removed, including an encapsulated tumor which was the size of a horse chestnut. Round-celled sarcoma. No recurrence in three and one-half years.

CASE XXXVIII.—Naegele.³⁸ In a child, aged three months, a tumor growing since birth in the lower portion of tongue pushed the tongue up and back. No ulceration. Section of tumor removed. Round- and spindle-celled sarcoma. Death from pneumonia in six days. Autopsy showed a diffuse sarcoma displacing the muscle fibers. No glands involved nor other metastases.

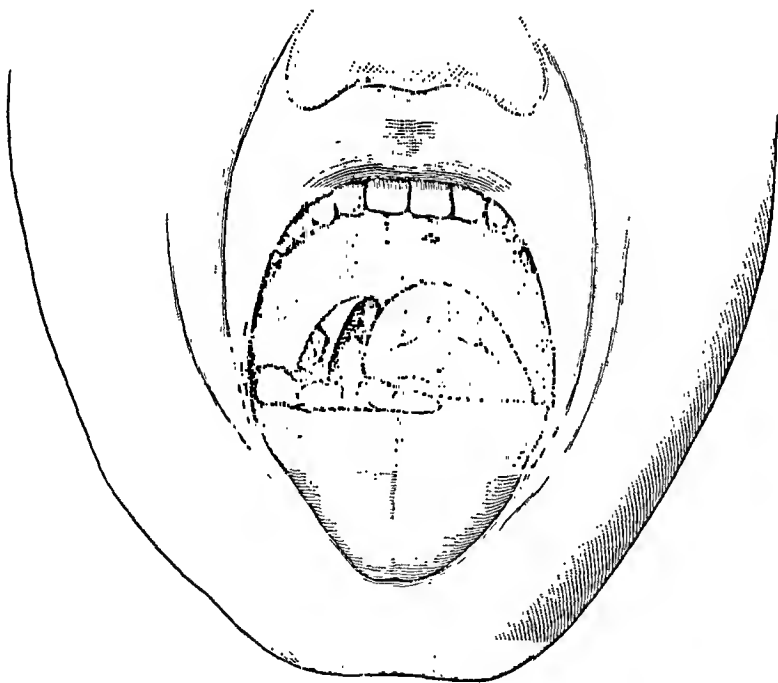


FIG. 7.—Spindle-celled sarcoma of the tongue. (Shambaugh.)

CASE XXXIX.—Shambaugh.³⁹ Male, aged thirty-eight years, could not give any cause for gradually increasing pain and swelling of tongue with marked emaciation during eight months. Tumor the size of a small hen's egg on the left side of the base of the tongue,

³⁷ Diseases of the Tongue, 1900, p. 302.

³⁹ AMER. JOUR. MED. SCI., 1902, cxxiii, 115.

³⁸ Inaug. Dis., Kiel, 1900.

completely filling the left side of the pharynx. Bled easily when touched. A small, firmer tumor occupied the right side of the base of the tongue as far forward as the papillæ. No ulceration. No enlarged glands. Soon after this an enormous hemorrhage nearly caused the patient's death. The large tumor was somewhat shrivelled; section removed showed a spindle-celled sarcoma.

CASE XL.—Fripp and Swan.⁴⁰ Male, aged twenty-six years, without history of syphilis or injury, developed a tumor in upper and posterior part of tongue with enlarged submaxillary glands. Iodides given without benefit and swallowing and breathing became difficult, so that in three months tracheotomy was performed. Two months later a smooth, firm, non-ulcerating tumor filled almost the whole pharynx. There was a large mass of lymphatic glands between the jaw and thyroid. Part of tongue containing tumor and mass of glands removed in one piece, September, 1899. Tumor measured 7 by 5 cm. Spindle celled sarcoma. Recurrence first noted in eighteen months. Operation for recurrence in tongue only two years after first operation. Six months later no sign of recurrence.

CASE XLI.—Chanu.⁴¹ Female, aged forty-two years, suffered without known cause for eight months from a painful tumor infiltrating the right side of tongue behind the circumvallate papillæ. Speech normal. Swallowing very difficult. No ulcer. Small movable painless glands palpable on both sides of neck. Removal of glands and ligation of lingual artery on left side of neck. Removal of glands and ligation of external carotid and branches right side of neck. Incision into pharynx and excision of part of base of tongue with tumor. Suture. Sarcoma of tongue and lymphatic glands; cells mostly small and round, a few racquet-shaped. Patient recovered perfectly. No sign of recurrence in nine months.

CASE XLII.—Fisk.⁴² Male, aged seventy-one years, without syphilitic history, bit his tongue. In ten months the right half of tongue grew until he could not close his mouth. No ulcer. No enlarged glands. Great pain. Cachexia marked. Excision of tumor, September 17, 1902. Small round-celled sarcoma. Two months later no recurrence.

CASE XLIII.—Matrisimone.⁴³ Female, aged fifty-five years, presented a tumor of right margin of tongue, which was several times excised, but recurred rapidly. Myxosarcoma from connective tissue; muscular bands not affected. Subsequent history not given.

⁴⁰ Guy's Hosp. Rep., 1902. lvii, 88.

⁴¹ Thèse de Paris, 1903, No. 302.

⁴² Annals of Surgery, 1903, xxxvii, 373.

⁴³ Policlinico Ser. Chirurg., 1903, No. 11, and Zentralbl. f. Chir., 1904, p. 604.

CASE XLIV.—Keenan.⁴⁴ Male, aged forty-seven years, noticed for three months slight pain and fulness at base of tongue, and later a firm globular tumor, 1.5 cm. in diameter, well back on dorsum of tongue to right of median line. No ulcer. No enlarged glands. Sections removed showed growth to be a small, round-celled sarcoma. Operation refused, but one month later performed elsewhere, the tumor being excised. Some weeks later a mass in the abdomen was noticed, which ultimately involved the stomach, duodenum, and pancreas and caused the patient's death in eleven months from his first symptoms. Abdominal tumor was of the same nature as that in tongue.

CASE XLV.—Cheatle.⁴⁵ Female, aged fifty-two years, noticed for six weeks a tumor right side tongue half-way back; no enlarged glands. Encapsulated tumor excised. Spindle-celled sarcoma. Recovery from operation. Subsequent history not given.

CASE XLVI.—Wiggin.⁴⁶ Female, aged twenty-three years, noticed for seven years a small nodule at back of tongue. A doctor pulled it off and cauterized the wound. Prompt recurrence of tumor on left side of tongue about one and one-half inches long. Tumor shelled out of capsule November, 1905. It was examined by four pathologists with following result: "Fibroma, benign" (Krumwiede); "fibroma, benign" (Dunham); "fibrosarcoma, only slightly malignant" (Jeffries); "fibroma, may recur locally" (Welch). Nine separate tumors shelled out from right side of tongue February, 1906; and a diffuse growth removed from scar on right side of tongue April, 1906. The results of pathological examination were: "Fibroma" (Krumwiede); "sarcomatous element in tumor" (Dunham); "sarcoma" (Jeffries); "fibroma, possibly rhabdomyoma" (Welch). Rapid recurrence after last operation. Trypsin treatment gave temporary relief, then continued growth.

I had an opportunity to examine this patient in January, 1912, and found the tongue practically normal, without evidence of tumor and scarcely a scar.

CASE XLVII.—Serafini.⁴⁷ Female, aged thirty-four years, noticed a tumor of the border of the tongue since she was twelve years old. It developed in the wound caused by a sliver of lead. A small tumor remained stationary for twenty-two years. Then began to grow. Ulcerating tumor easily bleeding; an enlarged gland in the submaxillary region. Excision of the tumor. Spindle-celled sarcoma of the interstitial type.

CASE XLVIII.—Schleinzer.⁴⁸ Female, aged fifty-four years, experienced rather sudden pain and difficulty in swallowing, followed in two weeks by copious expectoration and very bad breath. Ulcer with sharp edges on right margin of tongue. Enlarged glands

⁴⁴ Ann. of Surg., 1904, xxxix, 956.

⁴⁵ Jour. Amer. Med. Assoc., 1906, xlvii, 2003.

⁴⁶ Deut. Zeit. f. Chir., 1911, cix, 283.

⁴⁷ Med. Press and Cir., 1906, ii, 14.

⁴⁸ Rev. de Chir., 1909, xi, 242.

right side of neck. Extensive removal after temporary division of lower jaw. Lymphosarcoma. Later removal of gland from left side of neck showing metastasis. In five years no recurrence.

CASE XLIX.—Author's case described in the beginning of this article. Last operation May, 1911. Patient reports no evidence of recurrence January, 1912.



FIG. S.—Macroglossia (Comroe).

For the sake of comparison a brief abstract of the case recently reported by Comroe of macroglossia of the lymphatic type is here given.

Comroe⁴⁹ (Operator, Harrison). Female, aged three years, a child of healthy parents, was observed at birth to have a very large tongue, which increased rapidly after the first year, developing great papillæ and taking on a bluish color. After two years of age, fissures appeared and there were several hemorrhages, one of alarming character. The posterior half of the tongue appeared quite normal; the lips were swollen and excoriated, and pressed forward by the tongue, the mass of which prevented the incisor teeth from touching when the molars were closed.

⁴⁹ Cleveland Med. Jour., September, 1911, p. 743.

A section was removed for examination and found to be lymphangioma. "There was a marked overgrowth of connective tissue with profuse infiltration of white cells in the form of lymphoid tissue."

The anterior portion of the tongue was excised. Four months later the tongue was essentially normal, and the deformities of the jaw were much less marked.

THE INFLUENCE OF ORAL SEPSIS ON DIGESTIVE DISORDERS.

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AMONG the portals of entry for disease, the mouth is naturally the most important. It is the outer vestibule through which the food, drink, and air must pass before beginning their useful functions in the bodily economy; its warmth, moisture, and alkaline reaction offer the necessary conditions for the cultivation of septic products; and there is usually in the mouth plenty of culture material, in the form of food debris, etc., upon which they can grow.

As active etiological factors in digestive disturbances, I do not believe the different manifestations of oral sepsis have received merited attention.

Our enterprising friends, the laryngologists, have studied well the influence of disordered digestive processes upon the throat and postnasal territory, elucidating this part of the subject at length; while the ophthalmologists and aurists have attested their interest by numerous papers. The dentists, like watchmen on the towers, have continually sounded the alarm, and a few adventurous spirits have invaded the ranks of the medical profession, preaching oral prophylaxis from the housetops.

As to any extended or thorough literature covering the title of this paper, I have failed to find it, and the conclusions embodied herein are in a great measure deduced from my own investigations, and supported by fragmentary allusions gleaned here and there.

Before studying the effects, it might be well to enumerate the different organisms, pathogenic and otherwise, which at different times inhabit the mouth: *Bacillus buccalis maximus*, *Bacillus prodigiosus*, *Bacillus violaceus*, *Bacterium cerasinum*, *Bacterium coli commune*, *Bacterium gingivæ pyogenes*, *Bacterium termo*,

Iodococcus vaginatus, *Leptothrix buccalis*, *Leptothrix innominatus*, *Micrococcus gingivæ pyogenes*, pneumococcus of Friedlander, pseudodiphtheritic bacillus of Ronx and Yersin, *Proteus vulgaris*, *Sarcina aurantiaca*, *Sarcina lutea*, *Spirillum sputigenum*, *Spirochæta dentium*, *Staphylococcus albus*, *Staphylococcus aureus*, *Staphylococcus citreus*, *Streptococcus*, *Vibrio rugula*, and Vignal's bacillus.

As lengthy as is this list, there are many other varieties present not sufficiently studied to classify or name, and, notwithstanding their number, strange to say, this cavity is usually not very septic.

Formerly we were taught that the saliva possessed a bactericidal action, but this has been disproved by Sarinelli, who showed that while saliva was inimical to the *Staphylococcus pyogenes aureus*, it was so only to a negligible extent.

From experiments performed by Hugenschmidt, in Metchnikoff's laboratory, at the Pasteur Institute, we are led to believe that excessive sepsis is held down by the reciprocal action of the bacteria and their secretions upon each other. Moreover, actual invasion of the buccal cavity is prevented in the normal mouth by the activity of the phagocytes in the mucous membrane, and by the ability of the stratified pavement epithelium to continually shed and renew its superficial layers.

It may be truly said that the mouth is never out of service; but when, instead of being a proper entrance and "testing station" for all systemic and commissary supplies for nutrition and maintenance of heat as they are received into the body, and sent to that distributing centre, the stomach, it also becomes a repository for pus, where hordes of bacteria disport themselves in microscopic glee, proliferating day and night, developing ptomaines and toxins galore, we can easily understand the pathological possibilities of such a focus.

In the limited sense this study purports to cover, septic products in the mouth may set up digestive disturbances by direct absorption from the buccal walls; or, when swallowed, may either act locally upon the gastric mucosa, or may cause fermentation in the stomach or intestines.

The physiological functions of the tonsils are still in doubt, but to some extent they probably act as pharyngeal filters. I have in three instances seen attacks of acute appendicitis follow closely upon the heels of acute tonsillitis, and in each there was also pus around the roots of some of the teeth.

Inquiry among local surgeons failed to elicit any definite data in this respect, but I submit it as worthy of consideration. I might add as a postulate that, if enough nicotine can be absorbed from the buccal cavity alone to produce marked effects, it is entirely reasonable to conclude that pathological bacteria may be also absorbed to an appreciable extent.

Bunge and others have claimed that a not unimportant function of the gastric juice is the sterilization of the stomach. That this can be only partially true is shown by the continued activity of ptyalin before and until the stomach contents become thoroughly acidified. Moreover, according to Lucksdorff, the mouth bacteria constitute at least 3 per cent. of those found in the intestinal contents, where the stomach possesses normal secretory powers. It can be readily seen, therefore, that in achylic stomachs, or those where the hydrochloric acid is markedly deficient, this stream of pus, as it is poured down the esophagus and over the gastric mucosa, may directly kindle an acute gastritis.

This has been demonstrated to my satisfaction by numerous instances, where local gastritis yielded to treatment only after foul mouths had been righted.

Let me quote from Hemmeter: "The direct causes of the rarer idiopathic phlegmonous gastritis are unknown, . . . but, judging from anatomical specimens, are probably bacterial invasions of the submucosa, principally from pyogenic cocci, which find portals of entry through lesions in the superficial epithelium of the stomach, such as occur in most gastric diseases."

Also from Dr. John Fitzgerald: "As regards chronic gastritis, I think that we may take it as proved that it is often caused by swallowed microorganisms and pus. In these cases it is apparently not the microorganisms themselves, but their irritating products which set up gastric inflammation. This is especially true of the yeasts, which give rise to excessively irritating products."

Probably the majority of digestive disturbances arising from oral sepsis are put in motion by fermentations set up in the stomach and intestines. Among the most important are the lactic and butyric acid fermentations, and, as the lactic acid microorganism is invariably found in connection with tartar and pus pockets around the teeth, we see how impossible it is to cure a chronic fermentative gastritis or gastro-enteritis while reënforcements from an unhealthy mouth constantly aggravate the trouble.

With the hydrochloric acid absent or deficient, antiseptic medication amounts to but little, so long as the patient is swallowing countless fresh germs with each meal.

In gastric atony, dilatation, or pyloric obstruction, with delayed evacuation of the stomach contents, oral sepsis produces its maximum evil influence. Especially is this observed in old cases of pyorrhea alveolaris, where the pyogenic organisms, after leaving their "pent-up Utica" in the mouth, find a larger sphere of activity in the stagnant pool always present in the stomach. This fermentation continues with unabated energy in the alkaline and neutral secretions of the intestines, giving rise to flatulence, painful peristalsis, diarrhea, and various other intestinal ills.

Appropriate diet, lavage, and antiseptics can mitigate these

conditions, but no material nor lasting improvement may be expected until the "fountain head" is purified.

Another frequent source of gastric and intestinal disturbance arises from the continual dropping accompanying postnasal catarrh. The influence of this stream of mucus and muco-pus, consciously and unconsciously entering the stomach day and night has been unduly minimized; in fact, a widely known practitioner of this city recently expressed the opinion that the swallowing discharge from such source exerted no injurious effect whatever.

To disprove such a statement, let me ask my readers if they know of any patients with long-standing postnasal catarrh who do not complain of some digestive discomfort; or how many they have observed whose nutrition greatly improved after this constant dropping of mucus was abated.

My case records show many such instances; so many, that I am most careful not to give a too optimistic prognosis in any digestive complaint, coincident with postnasal catarrh, and accompanied by deficient hydrochloric acid secretion, unless intelligent rhinological treatment can also be accorded.

A somewhat extensive experience has convinced me that a large proportion of the indigestion met with among those who throng our clinics arises from postnasal catarrh or pyorrhea alveolaris. From either indifference, ignorance, or poverty these septic oral conditions are neglected, until some of the mouths they bring to us would have made old Augeas think his stables sanitary marvels in comparison.

Less than a month ago there was referred to me a supposed case of pellagra, a man, aged forty years, whose every tooth rested in a seething pool of pus, whose mouth was raw, whose stomach and bowels were upset, whose skin was rough and dry from malnutrition. After this man's mouth was put in decent order, and his alimentary tract permitted to recuperate from the ravages of the purulent host that so long held sway, he was absolutely transformed, leaving the hospital an apparently robust specimen of manhood.

An eminent surgeon told me a short time ago that he never willingly performed any operation on the alimentary canal in the presence of pyorrhea alveolaris. Some unsatisfactory results had taught him this lesson—a lesson being learned by many others.

How many clinics there are where every portion of the human anatomy is carefully investigated excepting the oral cavity. A perfunctory glance at the tongue, and then *away* from the mouth go these diagnostic sleuths, leaving undiscovered in many instances the chief clue to some obscure digestive malady.

In the study and treatment of the manifold diseases of digestion, we are often puzzled at seeming etiological inconsistencies, at therapeutic missiles that fail to reach the spot where we aim.

This brief paper is intended to emphasize the importance clini-

cally of aseptic mouths; to emphasize the malign influence of septic mouths upon the whole alimentary tract; and to suggest that we get in closer touch with our friends and co-workers, the dental surgeons, who can so often furnish us a practical solution of some of our vexed gastro-intestinal problems.

THE PROGNOSTIC VALUE OF THE UROCHROMOGEN AND DIAZO REACTIONS IN PULMONARY TUBERCULOSIS. A PRELIMINARY REPORT.¹

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IN 1882, Paul Ehrlich² first described his diazo reaction, and since that time the literature has abounded in records of the observations of various investigators concerning the test. As this paper deals only with the relation of the reaction to pulmonary tuberculosis, no reference will be made to the occurrence and significance of the test in typhoid fever, measles, scarlet fever, erysipelas, pneumonia, diphtheria, and pyemia.

Ehrlich,³ himself, considered this reaction to have great prognostic value in pulmonary tuberculosis, and thought that if it were present over a fairly long period of time, it prophesied an early death. However, there seems to be a great difference of opinion in regard to this matter.

Cornet⁴ states: "Further investigations of Lovinson, Brecht, Petri, Escherich, Penzoldt, Georgiewsky, Brehmer, Beck, and others, have modified the conclusions of Ehrlich to a certain extent. The reaction is indeed present in a large number of fatal cases of phthisis, especially during a considerable period previous to death. It is not invariably, however, of evil import. It may also be lacking in spite of very severe exacerbations of the disease."

Blad and Videbeck⁵ conclude that a pronounced diazo reaction is a sign of an unfavorable prognosis.

Giesler⁶ states that it is not found in a majority of cases, even in the third stage, and hence its value in prognosis is limited.

From a study of 663 cases of phthisis, Wood⁷ arrives at the conclusion that if the urine shows a continuous well-marked reaction, the prognosis is bad.

¹ Read at the Staff Meeting, U. S. A. General Hospital, Fort Bayard, N. M., October 3, 1911. Published with permission of the Surgeon General, U. S. Army.

² Zeit. f. klin. Med., iv, 285.

³ Loc. cit.

⁴ Acute General Military Tuberculosis, Nothnagel's Encyclopedia of Practical Medicine, p. 409.

⁵ Zeit. f. Tuberkulose u. Heilstadte, 1901, p. 412.

⁶ Ibid., 1902, p. 406.

⁷ Medical News, 1903, p. 631.

Lawrason Brown⁸ states: "The diazo reaction is recognized to have marked limitations in regard to prognosis. On the whole, however, if the patient has no kidney affection and has taken no salol or other drug which affects it, the constant occurrence of the diazo reaction may be considered as an unfavorable sign. The intensity of the reaction is of considerable import."

Michaelis⁹ believes that the presence of the diazo reaction indicates either that the process is extensive or that it will progress very rapidly, and that the prognosis is grave. A cure, he believes, is impossible, and improvement, if any, only temporary. Moreover, he suggests that a fatal result may be expected within six months after the reaction becomes persistently present.

Clemens, Rutimeyer, Frankel, Troje, Gundriss, Cuopf, Goldschmidt, and others have obtained positive results in a large number of fatal cases.¹⁰

Gwerder¹¹ discusses the extreme diversity of opinions held by different observers as to the prognostic value of the reaction. He says: "Whereas some consider the positive reaction as an almost certain sign of a bad course of pulmonary tuberculosis, and go so far as to even exclude patients with a positive diazo reaction from the sanatorium, other authors deny any prognostic value in the reaction, pointing out, not entirely without justification, the fact that, on the one hand, cases which pursue a bad course may never show the reaction, or only irregularly; and that, on the other hand, improving patients may have a positive reaction." With reference to these contradictions, he calls attention to the fact that there are some cases in which, as he has shown by his experiments, the Ehrlich body is excreted in the urine, without it being possible to demonstrate this by the usual method. He further states: "It is equally intelligible why one or another case, in spite of a positive test, may improve, if only for a short time, for, in fact, it is only the reaction which lasts a long time which should be considered as of evil omen; while the transitory reaction in any tuberculous patient may occur during the time of an exacerbation, or of a new attack. But such cases are, on the whole, to be regarded only as exceptions."

On the assumption that the content of the urine in Ehrlich's substance is important with reference to the severity of the case, and rises and falls with improvement or deterioration of it, Gwerder endeavored to determine quantitatively the amount of Ehrlich's substance contained in a given urine. He relied upon the fact that the Ehrlich body can be changed by oxidation into a substance which no longer gives a typical reaction, and used a weak solution of potassium hypermanganate (1 to 1000), which he added to the urine drop by drop, until there was no longer a positive diazo reaction. He found that in many cases the amount of potassium

⁸ Osler's Modern Medicine, iii, 355.

¹⁰ Simon's Clinical Diagnosis, p. 737.

⁹ Deutsch. med. Woch., 1899.

¹¹ Beitr. zur Klinik der Tuberkulose, xiii, No. 1.

hypermanganate necessary depended upon the severity of the case, and increased with increasing deterioration. Urine treated with a 1 to 1000 solution of hypermanganate of potassium on mixture with the Ehrlich reagent, gave only yellow or brown colors, according to the amount of the potassium hypermanganate. Brown shades, according to authors, are said to have nothing to do with the prognostic significance of the reaction. He, however, thinks that brown discoloration may serve as an indication of the severity of the disease, since we must assume that the brown coloration is caused by bodies which are chemically closely allied with the so-called Ehrlich substance. He states that a close relationship of these bodies with the Ehrlich substance must be assumed, and clinical and similar, although not so bad, prognostic importance must be assigned to them as to the Ehrlich substance. He calls attention to the increased power of reduction which the urines of tuberculous cases often show, and, almost without exception, of urines which give the diazo reaction, although it may occur in those urines in which Ehrlich's body cannot be determined by the usual reagent.

I have spoken at length of Gwerder's use of potassium hypermanganate in his tests, in order that it might not be confused with Weisz's "potassium permanganate" or "urochromogen" test, to be discussed later. Gwerder uses the potassium hypermanganate (K_2MnO_4) in combination with the Ehrlich sulphanilic acid solution; while Weisz uses the potassium permanganate ($KMnO_4$) alone.

Dr. Moriz Weisz¹² assigns as reasons for the contradictory opinions of observers as to the prognostic value of the diazo reaction the facts that the reaction requires a very exact technique; and further, that the sign of a positive reaction, the rose foam, even though the reaction is carefully done, allows for considerable scope of individual judgment, so that it is possible for one observer to call positive a reaction which another would pronounce negative. Then, too, the impossibility of exactly determining the nature of the substance causing the reaction, limits its value, so that one has to rely on empirical opinions.

As a result of six years of experimenting, Weisz concludes that the principal substance causing the diazo reaction is urochromogen. The principal part of the reaction, he states, is due to a low oxidation product of urochrome, the normal yellow pigment of the urine, and this substance he calls urochromogen. He also showed that one of the chief reasons for the uncertainty of the Ehrlich reaction was due to the fact that this principal substance, urochromogen, has an antecedent which does not give the diazo reaction. He found that by adding a solution of potassium permanganate to urines

¹² Münch. med. Woch., June 20, 1911, lviii.

containing urochromogen, the potassium permanganate was reduced, and a yellow color appeared. This test also permitted of the demonstration of the antecedent of urochromogen, the principal substance of the Ehrlich reaction, and was, moreover, far more constant than the diazo reaction. To this reaction he gave the name "urochromogen" or "potassium permanganate" test, and for six years he has used it, instead of the diazo reaction.

He states that urochromogen is found in the urine as a result of defective oxidation, which prevents it from becoming the finished product, urochrome. Such a condition of defective oxidation is present only when the katabolic processes of body metabolism are influenced by some toxin in the circulating blood, that is present in tuberculosis only when the lesion in the lung is sufficiently advanced to either (1) cause a massive invasion of toxin from the *Bacillus tuberculosis* into the blood stream, or else (2) to cause the organism to submit to an overwhelming power, and to cease its protective function which hitherto had kept the toxins in check.

Regarding the value of his test, Weisz states that it will be readily seen that the excretion of this substance goes hand in hand with an advanced and dangerous lesion, and that generally when it is found, marked physical signs which *per se* would lead to a poor prognosis are present in the lungs. On the other hand, he maintains that cases may be found in which the lesion in the lung is extensive, and which, from physical signs, would lead to a bad prognosis, but in which a negative urochromogen test shows that in spite of a large lesion, the productive power of the organism is ample to prevent the entrance of toxins into the circulation, and thus, that the case is not hopeless for the time being, at least.

He leaves open the question concerning the value of the reaction in regard to the point as to whether an occasional positive test should lead us to give a hopeless prognosis, and also whether we should distinguish between the constant and occasional appearance of urochromogen. His personal views are: (1) Patients who at the beginning of a course of treatment do not show a disappearance of urochromogen from their urine have a hopeless prognosis; (2) the transient appearance of urochromogen can be found in acute exacerbations of the disease, and is to be regarded as a symptom of progression of the tuberculous process; (3) a distinction between continuous and transient, constant, or occasional appearance of urochromogen should be made only as to the prospective duration of the disease; and (4) cases with transient excretion of urochromogen may, if external conditions are favorable, continue to live for several years, while the constant appearance of the reaction, especially when it is plainly becoming more intense, shows a rapid progress of the disease in the lungs and a hopeless prognosis. In brief, he regards as a sign of bad prognosis the appearance of urochromogen in the urine of any case of pulmonary tuberculosis.

He thinks that the further observation of the lives of the greater number of cases, who have shown positive diazo reactions and then apparently improved, would show that in spite of apparent improvement, they sooner or later succumbed to the disease.

At the suggestion of Colonel Bushnell, the Commanding Officer of this hospital, and realizing the truth of the words of Weisz, that "the value of such a reaction, which, so to speak, decides between life and death, cannot be too highly appreciated, as it would also give us a graduated measure for our therapeutic procedures," I undertook a study of the diazo and urochromogen reactions in the urines of patients suffering with pulmonary tuberculosis. I worked with the urines of cases whose physical condition was, with few exceptions, unknown to me, until after I had completed the series of tests. The urines were examined for ten successive days in August, and again in the same way in September. A diazo and a urochromogen reaction was done in each case.

As both Weisz and Gwerder had laid great stress on the question of the use of a proper technique in the diazo reaction, I used the utmost care in this respect. I added to 3 c.c. of filtered urine an equal quantity of a solution containing 50 parts of Solution A to 1 part of Solution B. The formulæ of these solutions are as follows:

Solution A: Sulphanilic acid, 1 part; 5 per cent. solution hydrochloric acid, 500 parts. Solution B: Sodium nitrite, 2.5 parts; distilled water, 500 parts. The mixture was then well shaken and 1.5 c.c. of ammonia added. As recommended by Simon¹³ and emphasized by Gwerder,¹⁴ I always studied the color of the ring which formed at the point of contact of the ammonia with the fluid before shaking. In positive cases the intensity of the color of this ring varies from eosin to a deep garnet, and is always more intense than the color of the shaken mixture or the foam.

The technique of the urochromogen reaction consists in adding 3 drops of a 1 to 1000 solution of potassium permanganate to 1 c.c. of urine diluted with 2 c.c. of distilled water. The appearance of a yellow color shows that urochromogen is present. The test is only considered positive when the solution remains clear. In each of the tests for urochromogen, I used a control tube of urine, diluted in the same way, and I would recommend that this procedure be followed in doing the test, as it enables one to distinguish very slight changes in color.

Table I gives the data regarding the cases examined. Table II shows the results of the test in each case. Especial attention is called to Cases 4, 7, 8, and 22, where the positive results seem to have a definite relation with the occurrence of hemorrhage, and to Cases 16 and 27, where the excretion of urochromogen seems to be associated with an intense and persistent headache in one

¹³ Simon's Clinical Diagnosis, p. 391.

¹⁴ Loc. cit

ease, and an attack of acute bronchitis in the other. In these 6 cases the appearance of the urochromogen in the urine seems to have some definite association with the complications mentioned.

TABLE I.—Data regarding cases examined.

Case No.	Duration of disease.	Class. ¹	Involvement. ¹	Maximum temperature.		Weight.		Sputum.	Complications.
				Aug.	Sept.	Aug.	Sept.		
1	10 mos.	I	I	101.0	99.8	203	198	Positive	
2	6 mos.	I	I	100.0	98.4	151	152	Negative	Malaria.
3	8 yrs.	I	I	100.0	100.4	108	108	Positive	
4	1 yr. 2 mos.	I	I	99.1	100.0	176	172	Negative	
5	5 yrs. 5 mos.	II	I	99.2	99.6	169	165	Positive	
6	1 yr.	II	I	98.4	126	...	Positive	
7	2 yrs. 4 mos.	II	I	99.4	100.2	163	165	Positive	
8	1 yr. 2 mos.	II	I	102.6	101.8	138	133	Positive	Syphilis; malaria.
9	6 mos.	II	I	98.4	98.4	129	133	Positive	Chronic bronchitis.
10	1 yr.	II	I	98.4	98.4	146	148	Positive	Syphilis.
11	1 yr. 7 mos.	II	I	98.4	98.4	147	145	Negative	
12	10 mos.	II	I	98.4	98.4	137	...	Negative	
13	1 yr. 1 mo.	II	II	98.4	98.4	117	127	Positive	
14	2 yrs. 3 mos.	II	II	99.4	98.4	139	138	Positive	
15	6 mos.	II	II	101.0	101.6	139	135	Positive	Cervical adenitis.
16	3 yrs. 9 mos.	II	II	100.2	98.4	212	209	Negative	
17	1 yr. 2 mos.	II	II	99.5	98.4	128	126	Positive	
18	7 yrs. 6 mos.	II	II	98.4	98.6	125	127	Negative	
19	1 yr. 3 mos.	II	III	100.2	100.2	137	136	Positive	Chronic pleurisy.
20	7 mos.	II	III	102.0	103	...	Positive	
21	1 yr. 8 mos.	III	II	99.6	99.6	138	136	Positive	
22	7 yrs. 5 mos.	III	II	101.2	99.0	...	110	Positive	Chronic laryngitis.
23	2 yrs. 8 mos.	III	II	101.6	116	...	Negative	Pott's disease.
24	4 yrs. 4 mos.	III	III	101.2	100.0	115	116	Positive	
25	1 yr. 3 mos.	III	III	103.0	103.0	110	109	Positive	
26	1 yr. 11 mos.	III	III	99.0	98.8	100	104	Positive	
27	8 mos.	III	III	100.2	103.2	147	147	Positive	Syphilis; chronic laryngitis.
28	3 yrs. 6 mos.	III	III	99.2	99.0	124	127	Positive	
29	3 yrs. 5 mos.	III	III	98.4	98.4	103	105	Positive	Pott's disease.
30	8 yrs. 6 mos.	III	III	98.4	99.0	117	114	Positive	Chronic laryngitis.
31	7 yrs. 8 mos.	III	III	98.4	99.0	144	151	Negative	Syphilis.
32	9 yrs. 3 mos.	III	III	98.4	98.6	133	133	Positive	Fistula from old empyema.
33	6 yrs.	III	III	99.6	99.2	108	106	Positive	Syphilis.
34	9 mos.	III	III	101.2	102.4	125	122	Positive	
35	1 yr. 7 mos.	III	III	102.0	101.2	104	103	Positive	Chronic laryngitis.
36	1 yr. 2 mos.	III	III	101.0	101.4	102	99	Positive	Chronic laryngitis.
37	3 yrs. 3 mos.	III	III	100.2	101.0	120	116	Positive	
38	3 yrs. 10 mos.	III	III	99.6	99.8	112	...	Positive	Abdominal fistula.
39	6 yrs. 9 mos.	III	III	102.4	105	...	Positive	

A careful study of Tables I and II will show that the cases showing urochromogen more constantly are, for the most part, those cases that are having the greatest temperature elevations and loss of weight. In other words, the cases which are showing the toxic influences of the germs of the disease to a more marked extent are the cases that have a more constant excretion of urochromogen. Case 21 is, according to the physical signs, a very advanced case, yet his temperature is not markedly elevated and urochromogen is absent from his urine. Time only will tell whether the difference between this man and his associates in the same class is that in his case, to use the words of Weisz, "the productive power of the organism is ample to prevent the entrance of toxins into the circulation," and that the giving of a more hopeful prognosis in his case is justified.

¹ Turban's classification.

Table III summarizes the results of the tests. In my series of cases there were positive diazo reactions in 29.1 per cent. of the cases; while 66.6 per cent. gave positive urochromogen tests.

A study of Table II would indicate that there is little or no relation between the extent of the tuberculous involvement and the appearance of the diazo and urochromogen tests in the urine. However, there is a definite relation between the positive findings and the acuity of the process, as is shown by Tables II and IV. The "bed patients" are, of course, the most serious, while the "ambulant" are the least serious cases, the "semi-bed patients" forming an intermediate class. The word "serious" refers to the acuteness and not to the extent of the process. There was a positive diazo reaction in none of the ambulant cases, in 15.7 per cent. of the semi-bed cases and 42.8 per cent. of the bed cases. The urochromogen test was positive in 45.4 per cent. of the ambulant cases, 47.3 per cent. of the semi-bed cases and 80 per cent. of the bed cases.

From the above it will be readily seen that both reactions occur more frequently in the severe cases, and with still greater frequency in the severest cases. The diazo reactions were more intense, and the urochromogen test even more so, in the more severe cases. Not only does the urochromogen reaction occur in a greater number of cases, but it occurs far more constantly than does the diazo reaction.

Weisz states that the excretion of urochromogen may follow the administration of an anesthetic or of tuberculin, but the opportunity to verify these facts has not presented itself.

The observation of these cases has not embraced a sufficiently long period of time to permit the drawing of definite conclusions regarding the probable duration of life after the beginning of the constant appearance of positive reactions. But the results so far seem to warrant the statements:

1. That the frequency and constancy of the appearance of the diazo and urochromogen reactions in the urines of cases of pulmonary tuberculosis is an index to the severity of the condition, a constant negative result pointing to a case that is doing well, while a constant positive result indicates a progressively downward case.
2. That the urochromogen test occurs more frequently, and is more constant than the diazo reaction. It is, therefore, a better index to the condition of the patient than the diazo reaction.
3. That the intensity of both the diazo and urochromogen reactions is of great import as an index to the severity of the condition, especially as a method of determining the difference in prognosis in cases which show the reactions constantly.

I desire to acknowledge my indebtedness to Colonel G. E. Bushnell and First Lieutenant C. E. Holmberg, Medical Corps, for valuable assistance rendered in reviewing the foreign literature.

TABLE II.—Results of tests.

Case No.	Class of patient.	Pulmonary condition.		August.				September.				Remarks.
				Diazo.		Urochromogen.		Diazo.		Urochromogen.		
		Class.	Involvement.	Positive.	Negative.	Positive.	Negative.	Positive.	Negative.	Positive.	Negative.	
1	Bed	I	I	0	10	0	10	0	10	3	7	Positive results in September followed a hemorrhage on September 16.
2	Bed	I	I	0	10	1	9	0	10	4	6	
3	Bed	I	I	5	5	10	0	6	4	10	0	
4	Bed	I	I	0	10	1	9	0	10	7	3	
5	Ambulant	II	I	0	10	0	10	0	10	0	10	Left August 22. "Improved." Positive result in August occurred on day of a slight hemorrhage. Bed patient in August. Ambulant in September.
6	Bed	II	I	0	8	2	6	0	10	3	7	
7	Ambulant	II	I	0	10	1	9	0	10	0	0	
8	Semi-bed	II	I	4	6	6	4	1	9	4	6	
9	Semi-bed	II	I	0	10	1	9	0	10	0	10	Has syphilis. Received a dose of salvarsan between conclusion of August and beginning of September tests.
10	Ambulant	II	I	0	10	4	6	0	10	0	10	
11	Semi-bed	II	I	0	10	0	10	0	10	2	8	
12	Ambulant	II	I	0	10	0	10	0	10	0	10	
13	Semi-bed	II	II	0	10	0	10	0	10	0	10	Sent to duty August 21. "Cured." Bed patient in August. Semi-bed in September.
14	Semi-bed	II	II	0	10	0	10	0	10	0	10	
15	Bed	II	II	3	7	5	5	2	8	5	5	
16	Bed	II	II	0	10	0	10	0	10	2	8	
17	Semi-bed	II	II	0	10	1	9	0	10	0	10	Bed patient in August. Ambulant in September. Bed patient after September 27, on account severe headache. Positive tests on September 26 and 27.
18	Ambulant	II	II	0	10	0	10	0	10	5	5	
19	Bed	II	II	0	10	1	9	0	10	5	5	
20	Bed	II	II	1	6	7	0	0	10	0	10	
21	Bed	III	II	0	10	0	10	0	10	0	10	Left September 13. "Improved." Died August 14, 1911.
22	Bed	III	II	0	10	5	5	0	10	6	4	
23	Bed	III	II	0	7	0	7	7	3	10	0	
24	Bed	III	II	1	9	3	9	7	3	10	0	
25	Bed	III	II	1	9	3	9	7	3	10	0	All positive results since hemorrhage August 21. Left September 1. "Improved."

Positive results occurred after an attack of acute bronchitis.
Left September 27. "Improved."
Left September 28. "Improved."

Bed patient in August. Semi-bed in September.

27	Bed	III	III	0	10	0	10	10	0	10	6	4
28	Ambulant	III	III	0	10	0	9	0	0	7	3	4
29	Semi-bed	III	III	0	10	1	5	5	0	8	3	5
30	Semi-bed	III	III	0	10	5	0	10	0	10	3	10
31	Semi-bed	III	III	1	9	3	0	7	0	10	1	9
32	Semi-bed	III	III	0	10	0	10
33	Bed	III	III	9	1	10	5	8	0	2	10	0
34	Bed	III	III	5	5	5	3	0	0	10	6	4
35	Bed	III	III	0	10	2	0	0	0	0	0	0
36	Bed	III	III	10	7	10	6	4	10	0	9	1
37	Bed	III	III	3	0	6	0	5	0	10	6	4
38	Bed	III	III	0	7	0	0	0	..	10
39	Bed	III	III	3	7	9	0	1

TABLE III.

	August.				September.				Summary.			
	Diazo.		Urochromogen.		Diazo.		Urochromogen.		Diazo.		Urochromogen.	
	Number.	Percentage.	Number.	Percentage.	Number.	Percentage.	Number.	Percentage.	Number.	Percentage.	Number.	Percentage.
Cases examined	38	..	38	..	34	..	34	..	72	..	72	..
Positive	12	31.5	25	65.5	9	26.4	23	67.6	21	29.1	48	66.5
Negative	26	68.4	13	34.1	25	73.5	11	32.3	51	70.8	24	33.3

TABLE IV.

	August.										September.										Summary.					
	Diazo.				Urochromogen.						Diazo.				Urochromogen.						Diazo.				Urochromogen.	
	Positive.		Negative.		Positive.		Negative.		Positive.		Negative.		Positive.		Negative.		Positive.		Negative.		Positive.		Negative.			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%		
Ambulant .	0	0.0	6	100.0	3	50.0	3	50.0	0	0.0	5	100.0	2	40.0	3	60.0	0	0.0	11	100.0	5	45.4	6	54.5		
Semi-bed .	2	22.2	7	77.7	5	55.5	4	44.4	1	10.0	9	90.0	4	40.0	6	60.0	3	15.7	16	84.1	9	47.3	10	53.6		
Bed .	10	43.4	13	56.5	17	73.9	6	26.0	8	42.1	11	57.8	17	84.2	2	16.7	18	42.8	24	57.0	34	80.0	8	19.0		

ON AGAR AS A VEHICLE IN INTESTINAL THERAPEUTICS.

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It is well known that Adolf Schmidt was the first to use agar-agar in order to increase the volume of the feces and thus relieve constipation. Agar itself not proving satisfactory, Schmidt combined it with *caseara sagrada* under the name of *regulin*.

Having used agar impregnated with various indicators (tincture of litmus, dimethylamidobenzol, etc.) successfully for chemical reactions in digestive examinations, it appeared to me that its employment could be extended for intestinal therapeutics. Dried agar is eliminated from the digestive tract undigested. While passing the canal it takes up a considerable quantity of fluid, and is then excreted in larger bulk than the original. This quality of agar makes it useful in conditions in which the feces appear in reduced quantity and are too dry.

In intestinal disturbances it is advantageous to apply a remedy that will cover a large area before being absorbed. This can be conveniently accomplished by using agar as a medicinal vehicle. For an agar-containing remedy will first absorb fluid and later liberate the medicinal substance through osmosis. This process takes place slowly, and in this way a large area of the intestines will take up the medicinal agent which has escaped from the agar through osmosis.

Another quality of agar which is advantageous, is its property of retaining fluids and thus increasing the bulk of and also partly softening the feces.

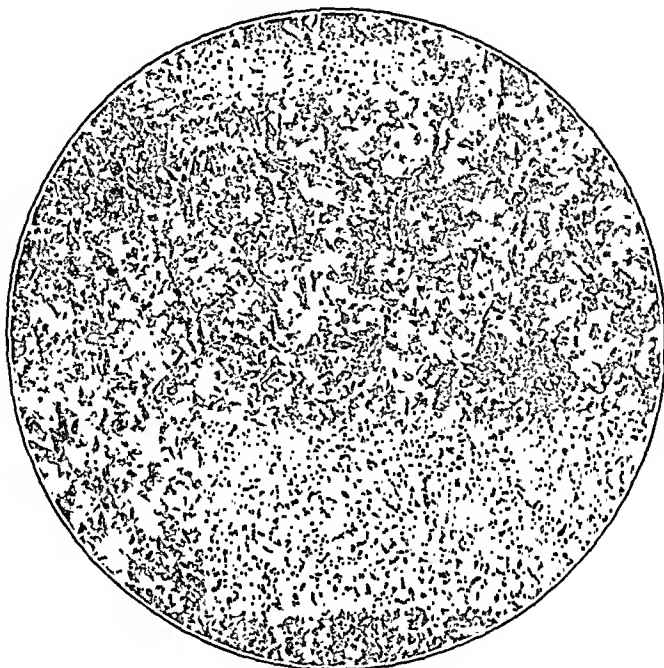
In constipation, therefore, agar as a medicinal vehicle appears at once as a valuable aid. For agar, impregnated with a laxative remedy, will increase the efficiency of the latter by the above-mentioned property of softening the stool.

But in diarrhea agar may also be profitably utilized. In combating diarrheal conditions we must take refuge in astringents, and in severe cases must resort to these in combination with opiates. Such remedies, however, occasionally act too pronouncedly and produce hardened scybala and constipation. In instances in which the mucosa of the bowel is not perfectly intact, but is inflamed or ulcerated, the constipation induced by the remedies given may be more harmful than the primary diarrhea. If, however, the astringent remedy is given in agar as a vehicle, these bad results of hardened feces are obviated. It is, therefore, evident that agar as a vehicle is also useful in diarrheal conditions.

Furthermore, in neurotic disturbances of the intestine agar can

be made to carry a sedative and impart it to a large area of the affected organ.

We can, therefore, make use of medicated agar in the most varied affections of the intestine, for example, in constipation, diarrhea, and enteralgia.



Photograph of rhubarb-agar flakes, natural size.

PREPARATION OF THE AGAR REMEDIES. To prepare medicated agar proceed as follows: The medicinal agent is dissolved in a boiling agar water solution, thoroughly mixed, then evaporated to the original dry agar volume. By knowing the quantities taken the medicinal agent can be standardized. The impregnated agar is then ground up into flakes.

I have used the following preparations with advantage:

1. Phenolphthalein-agar. Each level teaspoonful (1 gram) represents 0.03 gram (gr. $\frac{1}{2}$) of phenolphthalein.
2. Rhubarb-agar. Each teaspoonful represents 1 c.c. (℥ 16) fluidextractum rhei (U. S. P.).
3. Calumba-agar. Each teaspoonful represents 2 c.c. (℥ 32) fluidextractum calumbæ (U. S. P.).
4. Gambir-agar. Each teaspoonful represents 2 c.c. (℥ 32) tinctura gambir composita (U. S. P.).
5. Tannin-agar. Each teaspoonful represents 0.03 gram (gr. $\frac{1}{2}$) of tannic acid.
6. Simaruba-agar. Each teaspoonful represents 1 c.c. (℥ 16) tinctura simarubæ (U. S. P.).

7. Myrtill-agar. Each teaspoonful represents 1 c.e. (M 16) tinctura myrtill (U. S. P.).

8. Ipeacuanha-agar. Each teaspoonful represents 1 c.e. (M 16) tinctura ipeacuanhæ (U. S. P.).

9. Sumbul-agar. Each teaspoonful represents 1 c.e. (M 16) fluidextractum sumbul (U. S. P.).

Phenolphthalein and rhubarb-agar (1 and 2) can be conveniently used for the different varieties of constipation. One teaspoonful of either twice daily, after breakfast and supper, in some water, is the average dose. This, of course, may be increased or diminished according to the requirements of the case.

Calumba-agar (3) has proved valuable in cases of colitis (appearance of considerable mucus in the stool) with normal defecation. The average dose is one teaspoonful three times a day after meals, in some water.

Gambir-, tannin-, simaruba-, and myrtill-agar (4, 5, 6, and 7) I have found valuable in diarrheal conditions (acute and principally chronic). The average dose is usually one teaspoonful three times a day, after meals. Myrtill-agar I have also employed in diabetes mellitus, especially if complicated with enteritis.

Ipeacuanha-agar (8) I had prepared with the intention of administering it in amebic dysentery. I have, however, not yet tested it.

Sumbul-agar (9) I have employed in a considerable number of neurotic intestinal disturbances with seemingly good results. The dose was one teaspoonful three times daily after meals, in some water.

As a whole I can recommend the above various agar preparations as valuable remedies in intestinal therapeutics.

REACTIONS INDUCED BY ANTITYPHOID VACCINATION.

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WITH the object of determining the reactions induced by typhoid bacillus vaccines, we made a series of examinations of ten medical students, who voluntarily received the vaccination during the early part of the past year. We were especially interested in the

change in the number and proportion of leukocytes, but made such other determinations as were necessary to demonstrate that specific antibodies were actually produced. Finding that better results were obtained with a vaccine prepared at the Army Medical School, Washington, D. C., than one which was prepared from our own culture, we used vaccines supplied by Major Russell. This vaccine (No. 44) was prepared by cultivating a non-virulent strain of the typhoid bacillus on slanted agar for eighteen hours, then making a suspension of the growth in sterile salt solution and diluting it so that each cubic centimeter contained 1,000,000,000 bacilli. This was then sterilized at a temperature of 56° C. for one hour and its sterility tested by aërobic and anaërobic cultivation and by animal inoculation. After the addition of tricresol (to make a 0.25 per cent. solution) as a preservative the vaccine was placed in sterile glass ampoules, which were sealed by heat.

Artificial immunization against typhoid fever was first tried on lower animals by means of living cultures of typhoid bacilli. Among the earlier experimenters were Simmons and Fränkel (1886), Beumer, Chantemesse, Widal and Sanarelli.¹ In 1892 Brieger, Kitasato, and Wassermann² determined that the use of killed typhoid bacilli was quite as efficient in inducing the production of antibodies as were living bacteria. Pfeiffer's³ work in 1893 and the following year, in demonstrating the possibility of inducing marked bacteriolysis in the body (Pfeiffer's phenomenon) was a great stimulus to further research, as was also the work on agglutinins by Grubler and Durham in 1896. In 1896 Pfeiffer and Kolle,⁴ working together, and A. E. Wright⁵ independently, inoculated two men with typhoid vaccines. The laboratory evidence of the production of immunity was sufficiently great to warrant the application of the vaccination on a more extensive basis. In 1897 Wright⁶ reported the inoculation of eighteen persons, and the following year introduced antityphoid vaccination on a rather large scale among the English soldiers engaged in the Boer war in southern Africa. Certain unfavorable reports regarding the work in southern Africa caused a partial suspension of the work for a few years. In 1904, on the advice of R. Koch, it was introduced in the German army, and a little later reintroduced among the English soldiers through the efforts of Col. Leishman. In 1908 it was introduced in our own army, the vaccine being prepared under the direction of Major Russell, of the Army Medical School in Washington. The submission of our soldiers to vaccination was at first voluntary but was made compulsory in 1911.

¹ Handbuch der Technik und Methodik der Immunitätsforschung i, 723.

² Zeitschr. f. Hyg., 1892, xii, 137.

³ Deut. med. Woch., 1896, p. 735.

⁴ Brit. Med. Jour., January 30, 1897, p. 16.

⁵ Deut. med. Woch., 1896, Nos. 7 and 8.

⁶ Lancet, September 19, 1896, p. 807.

Clinical Evidence of Protection. The statistics of Wright⁷ on his vaccinations during the Boer war are based on 19,069 soldiers vaccinated as compared with 150,231 not vaccinated. Roughly considered, the vaccination reduced the incidence of the disease about 50 per cent. and the mortality almost 75 per cent. Later, with better technique in the preparation of the vaccine and having the vaccination consist of two or three injections, the results have been still better. According to a recent report of Leishman,⁸ based on 5473 persons vaccinated as compared with 6610 not vaccinated, the number of cases of typhoid fever and deaths from that disease was only about one-tenth as high among the former as among the latter. Instances in which protection was definitely proved, although on a smaller scale, are quite numerous.

Our vaccinations consisted of three subcutaneous injections in the arm at intervals of ten days, the first dose consisting of 500,000,000 typhoid bacilli and the other two of 1,000,000,000 each. The reaction may be both local and systemic in character. The local reaction begins usually in from four to five hours after injection and gradually subsides in three to five days. At its height it usually consists of an area of redness about 10 cm. in diameter, which is swollen and tender. Occasionally the axillary lymph nodes are also slightly enlarged and tender. A systemic reaction, consisting of one or more of the following symptoms, pyrexia up to 103° F., headache, malaise, insomnia, nausea, and in rare instances backache, vomiting, chills, herpes labialis, loss of weight, and albuminuria, also sometimes develops. These general symptoms begin usually in five to six hours after injection and disappear before the lapse of forty-eight hours. The reactions following the different injections in the same individual may vary somewhat, but taken on an average they become progressively less (see Table I).

TABLE I.

	Local redness and swelling 8 cm. or more in diameter.	Pain or tenderness in axilla.	No increase of temperature.	Temperature from 98.6 to 100.	Temperature from 100 to 103.	Temperature 103 or above.	Headache.	Backache.	Insomnia.	Nausea.	Chills.	Malaise.	"Soreness all over."
First injection . . .	10	5	4	6	0	0	2	3	4	2	3	6	1
Second injection . . .	10	2	3	7	0	0	1	1	0	0	0	2	3
Third injection (on basis of 9) . . .	9	0	2	7	0	0	0	0	0	0	0	0	0

⁷ Quoted by Russell, *The Military Surgeon*, 1909.⁸ *Royal Army Medical Corps*, 1909, xii, p. 166.

The frequency with which the signs and symptoms of the reaction developed in the individuals vaccinated, who were male students from twenty-one to thirty years of age, is given in the above table. Ten students received two injections, but only 9 were vaccinated a third time.

The mild character of the reaction is indicated by the fact that of more than 30,000 injections given to the soldiers of the United States Army, there was either no general reaction or only a mild one (temperature elevated but not up to 100° F., or merely headache and malaise) in about 95 per cent., and that in no instance were there any untoward results. In addition to the ten individuals of our series mentioned above, we also obtained a volunteer for vaccination who had had an attack of typhoid fever nine years previously. Following the first injection he had a severe local reaction consisting of swelling and redness of the entire upper arm and extending for two inches below the elbow. This inflamed area, which was very tender, continued for twenty-four hours. After his second injection the above-mentioned symptoms were even more marked and the individual had a temperature of 103.5° and was delirious for ten hours. In consideration of the severity of these reactions it was not thought advisable to give the usual third injection. Russell also reports more severe reactions in those who have previously had typhoid fever.

The reactions upon which the immunity depends or by which it may be measured may be divided into leukocytic, opsonic, phagocytic, agglutinic, and bacteriolytic. That the bacteriolysins are increased can easily be determined by the method of Pfeiffer. The bacteriolytic tests are, however, very unsatisfactory, inasmuch as no method has yet been devised by which the amount of bacteriolysins may be accurately determined. Although some observers⁹ have demonstrated that there is a marked increase in the opsonins, determination of the opsonic index is rather unsatisfactory. Somewhat more satisfactory is the estimation of the power of phagocytosis by the dilution method of Neufelt. Using this method, Russell¹⁰ has found that, beginning about the fifth to eighth day after the first injection, there was a rapid rise in the power of phagocytosis, reaching its height in about three weeks, when the phagocytic titer was one to two, occasionally five or six, thousand times as high as that of normal blood, after which it gradually declined until at the end of one year it was again normal. The agglutinins begin to increase at about the same time as the opsonins, as determined by the power of phagocytosis, and rise rapidly until, at the end of three or four weeks, it is possible to get agglutination (Widal reaction) with a dilution of blood serum 500 to 5000 times, or in some cases even 20,000 times. After

⁹ Jour. of Med. Research, June, 1910, xxii (New Series, xvii), No. 3, p. 435.

¹⁰ Boston Med. and Surg. Jour., January 5, 1911, clxiv, No. 1, p. 1.

this time it gradually declines, although it may still be possible to secure agglutination with a dilution of 1 to 100 at the end of a year.

Although a number of investigations relative to the degree of immunity as measured by the factors just mentioned have been made, we have found no record of a study of the leukocytic reaction following antityphoid vaccination in the human being. With the object of making such a study, careful leukocyte counts, both total and differential, were made of the ten subjects of our experiment. All of the counts were made at a time to avoid, so far as possible, the influence of digestion. Controls made by injecting as much salt solution and tricresol as is found in one dose of the vaccine did not give any leukocytic reaction.

Table II gives the average leukocyte count (total and differential) of the ten persons as determined before and at different times after the three injections.

TABLE II.

FIRST INJECTION.

Total and percentage of various types of leukocytes.

	Total number leukocytes.	Polymorpho-nuclear neu-trophiles.		Small lymphocytes.		Large mono-nuclears.		Eosino-philcs.		Transi-tionals.	
		No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Just before . . .	8400	5088	60.7	2544	30.0	424	5.0	137	2.8	132	2.7
One day after . .	10360	7148	69.3	2020	19.5	736	7.1	176	1.7	124	1.2
Two days after . .	8680	5900	67.6	1300	15.0	868	10.0	195	2.6	130	1.5
Three days after .	8130	4376	61.2	2057	25.3	772	9.5	138	1.7	162	2.0
Four days after . .	7140	3806	58.3	2070	29.0	685	9.6	164	2.3	57	0.8
Five days after . .	7111	4338	61.0	1586	22.3	704	9.9	185	2.6	92	1.3
Six days after . .	7210	4297	59.6	1859	25.8	576	8.0	331	4.6	201	2.8
Seven days after .	7960	5150	64.7	1926	24.2	562	7.1	127	1.6	166	2.1

SECOND INJECTION.

Just before . . .	6510	3647	54.8	2070	31.8	560	8.6	160	2.6	104	1.6
One hour after . .	7433	4159	57.3	2378	32.0	520	7.0	74	1.0	170	2.3
Six hours after . .	13540	9522	70.4	2978	22.0	947	7.0	121	0.8	119	0.8
One day after . . .	9280	6958	71.0	1959	21.0	55	0.6		
Two days after . .	7911	5505	69.6	1379	17.4	688	8.7	63	0.8	158	2.0
Four days after . .	7000	4179	59.7	1799	25.7	749	10.7	98	1.4	98	1.4
Seven days after .	6311	4077	59.0	2142	31.0	463	7.0	276	0.4	138	2.0

THIRD INJECTION.

Just before . . .	7742	4830	62.4	1455	18.8	836	10.8	155	2.0	155	2.0
One hour after . .	9600	6375	66.4	1920	22.4	499	5.2	192	1.2	132	2.0
Two days after . .	7400	4884	66.0	1659	22.4	444	6.0	59	0.8		
Four days after . .	6400	3667	57.3	1536	24.0	723	11.2	256	4.0	211	3.3

Chart I shows in a graphic way that the increase and decline in the total number of leukocytes occurs relatively about the same time following each injection. The degree of leukocytosis was highest following the first injection, and was successively less for the two subsequent injections. The curve following the second injection is the most representative one, inasmuch as several counts were made at short intervals following this injection. It indicates that the rise in the number of leukocytes in the peripheral blood is rapid and probably at its height in about six hours when the average count was 13,540 as compared with 6510 just before the injection. This corresponds to the time when the subjective symptoms are just beginning. The total count rapidly falls again, to reach the normal level on the second or third day after injection. In one instance the leukocyte count raised from 7200 just before injection to 8600 one hour later and 22,800 six hours after injection.

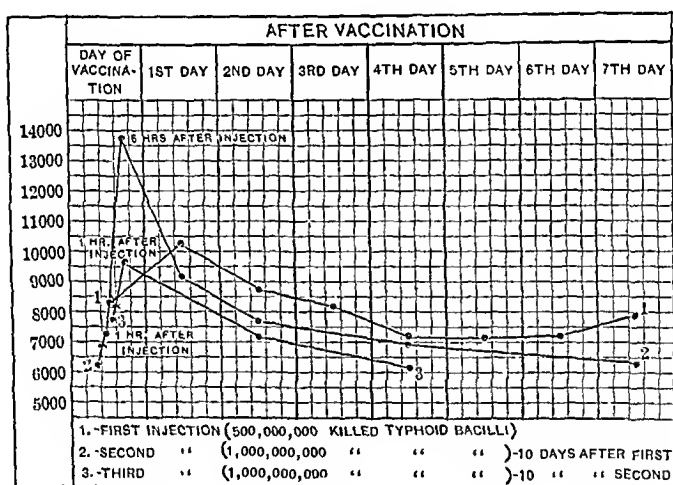


CHART I.—Total leukocyte count following antityphoid vaccination.

Chart II represents in a graphic way the total leukocyte count and the total number of each of the different types of leukocytes following the several injections. It will be noticed that the increase in the total number of leukocytes is due almost entirely to an increase in the number of the polymorphonuclear neutrophile leukocytes and the large mononuclears; the small lymphocytes the transitional cells and eosinophiles remaining about the same. It will also be noticed that the fall in the number of neutrophiles is more rapid than that of the total count, due to the fact that the large mononuclear counts remain rather high for from four to seven days after the injection.

Chart III represents graphically the percentage of the different types of leukocytes following the several injections. Considering

the curves given in Chart II, it is very apparent that the fall in the percentage of small lymphocytes, due to a corresponding increase in the percentage of the neutrophils during the first six hours after injection, caused a slight decrease in the percentage of the large mononuclear leukocytes. The percentage of the latter rose, however, to above normal, even while the percentage of the neutrophils was still high. The percentage of the large mononuclears, moreover, continued to remain above the normal even after the total count had become normal.

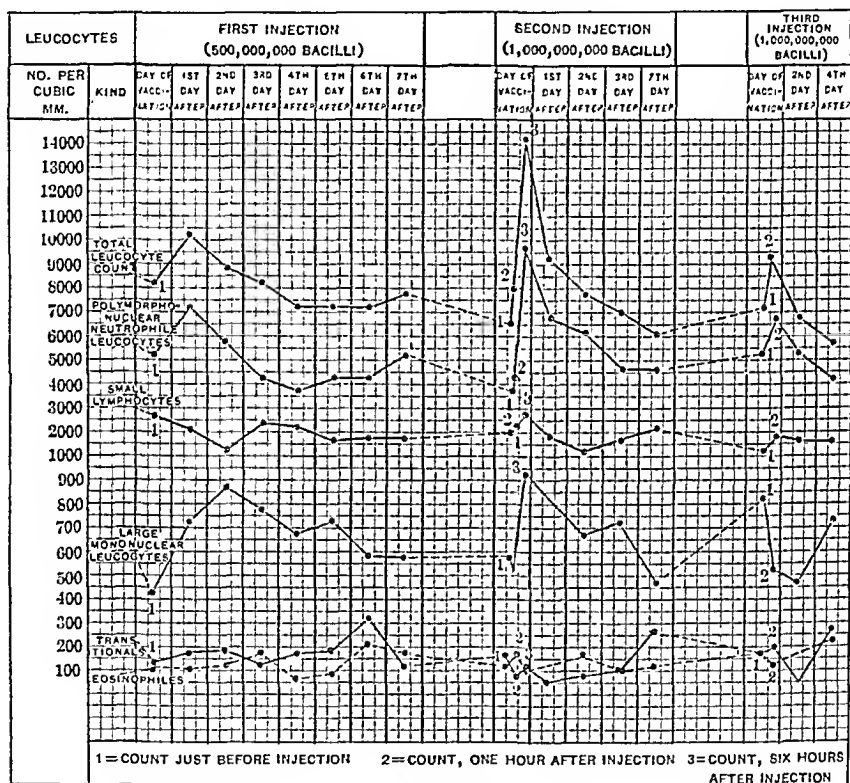


CHART II.—Leukocyte count, total and differential, following antityphoid vaccination.

It will be noted that there are two things about the leukocytic reactions that stand out prominently—(1) the high leukocytosis following injection of the vaccine, and (2) the considerable increase, both relative and absolute, in the number of large mononuclear leukocytes.

The increase in the total leukocyte count is of interest, inasmuch as there is usually no leukocytosis in uncomplicated cases of typhoid fever. It is due principally to an increase in the number of polymorphonuclear leukocytes. Such may readily be explained by the rather marked local reaction induced by the vaccine.

The increase in the number of large mononuclear leukocytes is, however, we believe, of more significance. The large mononuclear cells mentioned all had the same general appearance, but varied in size. A few of them were about the size of the polymorphonuclear leukocyte, but most of them were two to three times as large. The nucleus was usually slightly eccentric, but not peripheral, there being a thin ring of cytoplasm entirely around it. The diameter of the nucleus was usually about one-half the

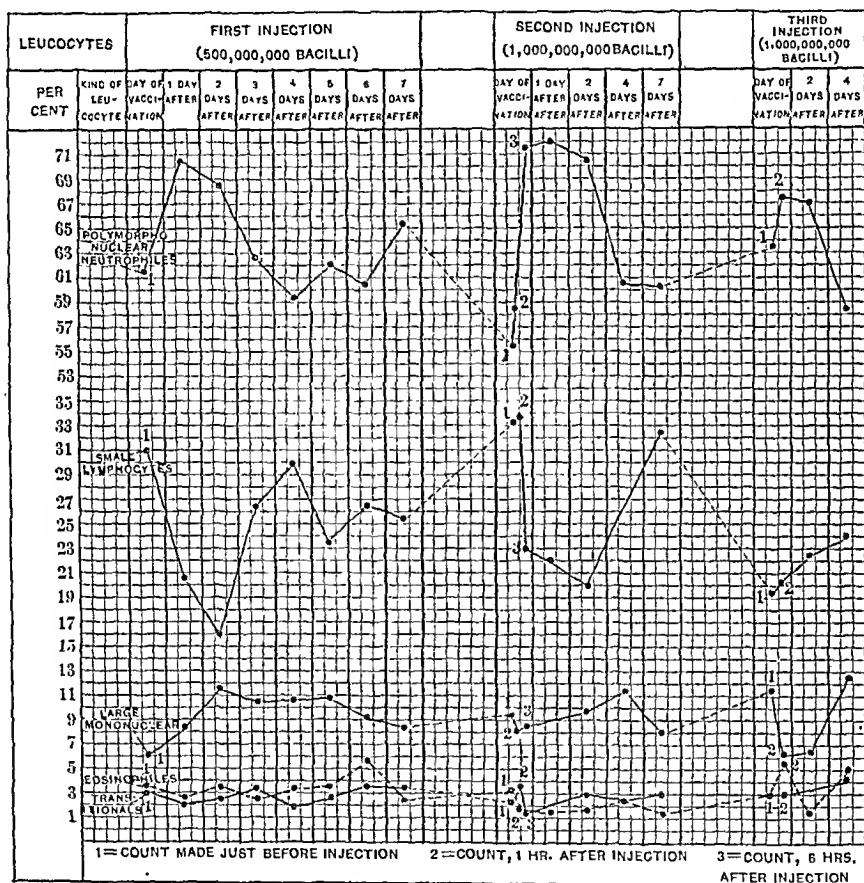


CHART III.—Differential leukocyte count following antityphoid vaccination.

diameter of the whole cell. It was stained deeply blue, being of about the same intensity as the nucleus of the small lymphocytes. The cytoplasm was of a paler blue than the nucleus, but not purplish. There were no definite granules in the cytoplasm, but it was occasionally noted that there seemed to be a very slight fibrillar character to it. At times it was noted that the nucleus was rather indefinite in outline and merged imperceptibly into the surrounding cytoplasm. The stain used was eosinated or erythrosinated methylene blue.

Various observers have noted that there is an increase in the number of the large mononuclear leukocytes in typhoid fever and during convalescence from that disease. Thayer,¹¹ on analyzing the blood findings of 832 cases of uncomplicated typhoid fever, found that the large mononuclear leukocytes represented on an average 12.4 per cent. of the leukocytes during the first week of the disease, 14.4 per cent. during the fourth week, 16.8 per cent. during the eighth week, at about which percentage it remained until after the fifth week of convalescence.

De Sandro,¹² conducting certain experiments in fatigue with dogs, rabbits, and guinea-pigs, and using "typhoid toxin" as a test of resistance, found that, after injection, there was an initial leukopenia, followed by a leukocytosis, at first of the polymorphonuclear type and later of the mononuclear (especially large) type. Of importance is the observation that in the fatigued animals the initial leukopenia was more marked and prolonged and the subsequent leukocytosis (both polymorphonuclear and mononuclear) was less intense and persistent than in the normal controls. He also found that the influence of fatigue caused the agglutinins to develop less rapidly and to a less extent than under normal conditions.

SUMMARY AND CONCLUSIONS. 1. Statistics based on a large number of cases show conclusively that antityphoid vaccination confers a marked degree of protection against typhoid fever.

2. The injection of typhoid vaccines induces a local reaction in all cases and a general reaction in some cases.

3. A previous attack of typhoid fever apparently causes the reaction to be more severe than is observed in individuals who have not had typhoid fever.

4. Antityphoid vaccination causes a marked increase in the specific agglutinins, opsonins, and bacteriolysins.

5. The injection of typhoid vaccines causes a marked polymorphonuclear neutrophile and large mononuclear leukocytosis.

6. The marked increase (both absolute and relative) of the large mononuclear leukocytes in the peripheral blood is the only leukocytic change which is common to both clinical typhoid fever and antityphoid vaccination.

7. Such occurrences suggests that these leukocytes have something to do with the formation of antibodies concerned with the production of antityphoid immunity.

8. It seems well worth while to attempt experiments on the artificial production of large mononuclear leukocytosis and to see what relation such may have to the production of antibodies in the presence of typhoid infection or antityphoid vaccination.

¹¹ Johns Hopkins Hosp. Rep., 1900, viii, 487.

¹² Riforma Med., 1910, xxxv, 841 to 871; abstract in Journal of Amer. Med Assoc., September 17, 1910, p. 1064.

A CASE OF BRAIN TUMOR SUCCESSFULLY LOCATED BY
MEANS OF THE X-RAYS.

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THE following case is reported because of the exceptional interest and importance of the x-ray picture. The tumor, which had undergone calcareous change, was clearly shown in the skiagram, and was removed. So far as we know, no case of brain tumor, in which the shadow was so clearly shown, has as yet been reported. As is well known, the x-rays are usually not of value in localizing these growths. In the present instance success was doubtless due to the fact that the tumor belonged to the class commonly known as psammomata, and was of very unusual size.

J. B., aged seventeen years, male, white. In early life, between the eighth and fifteenth years, the patient had had epileptic attacks, in one of which he fell and struck his right parietal region. This injury was thought to have some relation to his subsequent disorder. Following this fall the left arm and leg were affected with numbness and partial loss of power, which cleared up only after a long period. When aged fourteen years, the boy had a long attack of typhoid fever, after which he had no more epileptic attacks. In 1907 he was bitten by a dog, supposed to be mad, and took the Pasteur treatment.

The first symptoms of organic brain disease began one year before the patient came under our care. He began carrying his head to the right side, and had a sense of stiffness in the neck. Later he began to have an awkward gait, and his vision failed. There seems to have been little if any headache, at least no continuous headache. There had been some vomiting.

On admission to hospital the boy's condition was as follows: His gait was peculiar, the patient having a tendency to go toward the right side, holding his head rotated toward the right. He could walk without assistance across a room, but had difficulty in turning. His vision was evidently defective. There was no true loss of power in either the arms or legs. The knee-jerk was exaggerated on the left side and there was slight ankle clonus on the same side. On the left leg below the knee there was impaired sensation for touch, pain, heat, and cold. Elsewhere sensation was normal. None of the cranial nerves was involved, with the exceptions to be noted. The intelligence was clear, but possibly

a little sluggish. There was no ataxia of the arms, no pain in the extremities. No speech defects.

Dr. Philip H. Moore reported moderate choked disk on both sides, more marked on the left. Media clear. No hemorrhages. Pupils reacted sluggishly to light and accommodation. Right external and superior oblique muscles showed restricted movements.

Dr. Walter Roberts reported no impairment of hearing. The Wassermann test was negative. The patient's general health was good; lungs, heart, and kidneys normal.

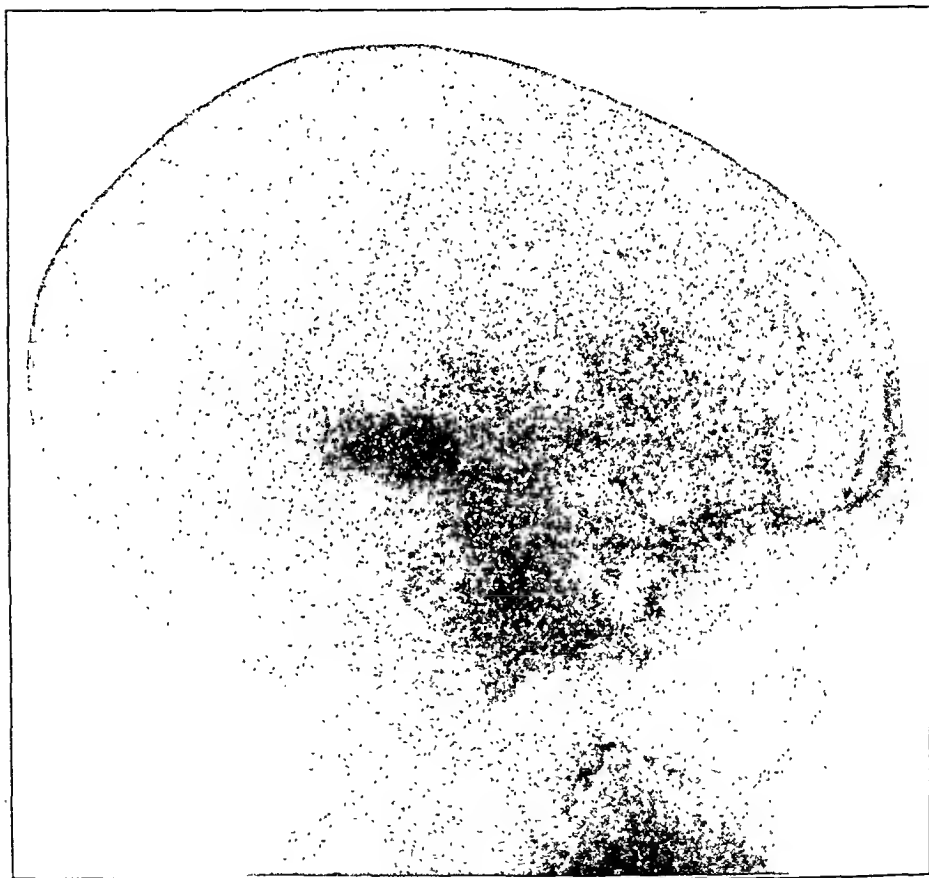


FIG. 1.—X-ray picture showing shadow of a brain tumor in the region of the temporal lobe.

The x-ray picture, taken by Dr. H. K. Pancoast, showed a very remarkable shadow. It was almost rectangular in shape, about 4 cm. long by not quite 2 cm. wide, and in the region of the temporal lobe (Fig. 1).

The patient was seen later in consultation by Dr. Dercum, at which time we decided on an operation, which was performed by one of us (Dr. Hammond) on June 6, 1911. The opening was made

directly over the spot indicated by the x-rays, that is, in the lower part of the right parietal bone, which was found extremely thin. As soon as the opening was made the membranes bulged under great tension. When these were incised a cyst was entered, the fluid escaping in a large quantity and under pressure. Deep within this cyst cavity a hard bony mass was felt; this was also palpated by Dr. Charles H. Frazier, who witnessed the operation. This mass was attached deeply at its posterior part, and was freely movable at its anterior end. On account of its deep attachment it was decided not to attempt to remove the tumor at that time, but to wait and do a second operation, in the hope that, following the line of least resistance, the growth would tend to present at the opening in the skull.

The patient's recovery from the operation was prompt and most satisfactory. In fact, all his symptoms disappeared so completely, that it was difficult to believe, except from the testimony of the x-rays and of two highly competent surgeons, that he still carried a hard bony mass, as large as a pullet's egg, in the interior of his brain. His staggering gait was gone, the stiffness of his neck muscles, and consequent rotation of his head, disappeared, and his eyesight became practically normal. Two weeks after operation Dr. Moore found the disks much more clearly outlined, although there was still some haziness about the margin of the left. Pronounced choking had practically disappeared, and the faint outline of the cups was seen. Both nerve heads were pale in color, veins no longer engorged, and arteries normal. The retinae showed numerous gray opacities, but much less cloudiness and swelling than before the operation. In short, the papillary edema had yielded promptly to decompression.

At this time, however, there was observed some slight astereognosis, such as inability to recognize a key and other objects placed in the left hand; but there was no anesthesia of any kind. The left knee-jerk was still exaggerated, and there was a slight Babinski reflex of the left great toe.

The patient continued in this favorable condition for the six weeks that he remained in the hospital after operation. He seemed so well that he was then allowed to go home in the interior of the State, still under careful supervision and direction. All went well for about another month, when it was observed that he was again losing sight, holding his head awry, and walking to one side. He was accordingly brought back to the hospital. On readmission his condition was very much as when first seen. All his symptoms had returned, and there was nothing to do for the boy but to operate.

At this time Dr. Moore made a very careful study of the visual fields and eyegrounds, and reported as follows: "Pupils large, round, and equal, reacting moderately to light and convergenc.

Rotation of globes in all directions normal, with only slight restriction in the extreme temporal movement of the right eye. Media are clear. The right eye has a pale nerve head with distinct margin. The physiological cup is lost. The vessels seem somewhat reduced in size from normal. The retina is slightly cloudy in the lower central area. In the left eye the nerve is less pale than in the right, the nasal margin is hazy, and there is a swelling of possibly one diopter. The vessels present no great departure from normal. The retina is hazy in places, but there are no hemorrhages. The macular region is undisturbed. Vision (without glasses) for the right eye is $\frac{2}{100}$ and for the left eye is $\frac{2}{40}$. With glasses the vision for the right eye is $\frac{2}{50}$ and for the left eye $\frac{2}{30}$. The restriction of the fields of vision is shown by the accompanying charts, and careful plotting of the color fields shows an interlacing suggestive of hysteria."

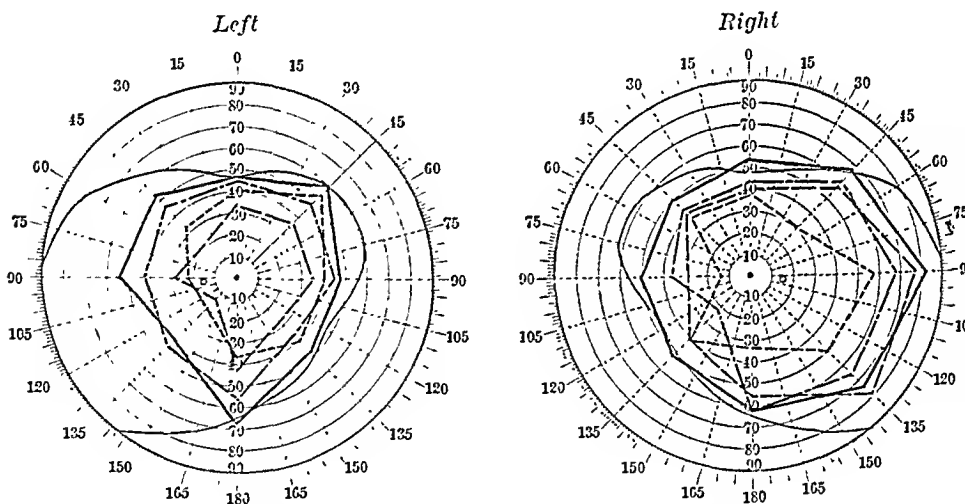


FIG. 2.—Perimeter charts showing restriction of the visual fields and interlacing of the color fields. Solid line = white; — — = red; - - - - = blue; --- = green.

One of us (Dr. Hammond) performed the second operation on August 19, more than two months after the first. The tumor was found *in situ*. It had a very peculiar feel to the finger, being like a rather rough stone, deep within the right hemisphere. It was taken out, however, in separate masses, or lobules, which came away without breaking. In other words, it consisted of several large masses and some smaller ones, closely packed together (almost like a nest of gallstones).

Description of Operation. The principles of asepsis were carried out by shaving the head, cleansing, and protecting the cavities accessory to the brain. Under ether anesthesia a free semilunar incision was made through the scalp and pericranium above and

1½ inches posterior to the right auricle, and the flap was reflected forward. A large trephine opening was made through the parietal bone, which was unusually thin; so thin, indeed, that the opening was additionally enlarged by paring off bone with the ordinary sized curved scissors. Immediately on removal of the bony plate internal pressure was so great that a large protrusion filled the opening.

The layer of brain substance beneath the dura was flattened and thinned from the pressure of the fluid in the cyst, which was encapsulated and superficial to the growth. After the rupture of the cyst wall and escape of its fluid contents, the tumor could readily be felt deeply seated above the tentorium and apparently adherent to the falx cerebri in a thin capsule of its own. It was irregular in outline, presenting to the sense of touch at least three distinct nodules. It was not difficult with a pair of long tissue forceps to grasp and remove each of these nodules separately. Hemorrhage, which was not excessive, was controlled by gauze packing. Drainage was inserted, the dura and pericranium carefully approximated over the convolutions, and the scalp sutured. The wound healed by primary union.

The patient stood the operation fairly well, but his condition was never as favorable as after the first operation. He began to fail about the sixth day, developing what was probably a uremic condition, for albumin and casts appeared in his urine, and on the eighth day he had a convulsion. From this he never fully recovered, and died on the same day. An autopsy unfortunately was refused.

It is of interest to note that the patient had been seen and examined by Dr. Charles W. Burr almost one year before he came under the care of one of us (Dr. Lloyd), and that Dr. Burr's notes closely correspond to ours. At that time, however, Dr. W. C. Posey reported a left homonymous hemianopsia, but this was not present at any time when the patient's eyes were examined by Dr. Moore, except that the left half of the right field was somewhat narrowed. In this respect there had evidently been some change in the interval of a year.

The location of the shadow in the x-ray photograph indicated a tumor within the posterior part of the right temporal lobe. It was too low to be in the parietal, or parietooccipital area. This we verified by comparing it carefully with the cast of a brain. This situation may indicate that this tumor, as in the case of most psammomata, sprang from the choroid plexus, and the cyst may even have communicated with the middle horn of the lateral ventricle. If this was so, we succeeded in tapping the ventricle without knowing or intending it. The absence of localizing symptoms is accounted for by the fact that this is a comparatively silent region of the brain. If the growth had been on the left side we should doubtless have had some speech defects. It was too far away to

involve the internal capsule, except a small portion of the sensory paths, as indicated by the anesthesia of the left leg below the knee. The patient's gait was somewhat like that caused by a cerebellar lesion, in the tendency to go to one side, but it was not a true cerebellar ataxia or titubation. We have no satisfactory explanation to offer of the astereognosis of the left hand, unless the tumor, as is often the case with brain tumors, caused more widespread pressure and interference with function than would appear probable from its location.

The microscopic sections were made by Dr. Ellen Corson White, who had some difficulty in decalcifying the material. These sections have been very kindly examined by Professor Allen J. Smith, who gave the following opinion:

"Section of brain tumor submitted by Dr. Lloyd, showed scarcely any matrix, but a great number of concentric psammoma bodies, which were merged in discrete and large fields, as if united after formation into a mass by the deposit of an intervening silicious material of the same character as that in the discrete bodies. In preparing the material for sections, Dr. White had found it impossible to decalcify, which was evidently dependent upon the fact that the concretions were not of plain calcareous nature, but of sand or silicious character. The little stroma recognizable which had refused staining and clear differentiation, probably partly from the action of the decalcifying agents, was evidently of a fibrous nature. From the deep location of the tumor the writer believes the growth probably started from the fibrous tissue of some of the bloodvessels of the cerebral substance."

The opinion of pathologists seems generally to be that these psammomata usually spring from the choroid plexus or pineal gland. Brain sand, as it is generally called, is not infrequently found in this location. The striking characteristic of the present case is the very large size of the psammoma and its great density. Tumors of various tissues, however, such as sarcomata, tuberculomata, fibromata, and lipomata, may undergo some calcareous change, but the change is seldom so complete. Two recent German writers, Zuckermann¹ and Hecht,² reporting such calcareous tumors of the brain, suggest that they may be teratoid or of the nature of dermoids, but this suggestion is not original, for dermoid tumors containing bone, teeth, and hair, have been found in the pituitary body and in the lateral ventricles.³

The x-ray picture in this case is a remarkable one, showing the shadow of the tumor very plainly, also the convolutions both of the cerebrum and of the cerebellum. This clear shadow is, of course, due to the hard bony nature of the tumor. We are not aware that

¹ Virchow's Archiv, 1911, Band ccciii, Heft 2, S. 161.

² Ibid., S. 165.

³ Beck, Zeitsch. f. Heilkunde, 1884; Gowers, Dis. New Syst., 2d ed., xi, 499, footnote.

any skiagram of a brain tumor has yet been published as remarkable as this one, an opinion expressed also by Dr. Pancoast, who took the picture. In looking at this skiagram we were struck with the clear delineation of the convolutions, and even thought that they showed some degree of flattening or pressure. This suggests a possibility in future cases in which no tumor shadow may be produced. It would, indeed, be interesting and important if we could attain such skill in interpreting skiagrams of the brain as clearly to determine the action of undue pressure beneath the convolutions.

THE RÖNTGEN RAYS IN HYPERTROPHIED PROSTATE: A THERAPEUTIC STUDY.¹

BY JAMES W. HUNTER, JR., M.A., M.D.,

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A CASUAL glance at the enormous literature upon the treatment of hypertrophied prostate would lead one invariably to the conclusion that this is a disease amenable to a great diversity of procedures and consequently likely to give the attending physician but little trouble. Upon further investigation, however, especially when one has had some experience of his own, we must conclude that here, as elsewhere, when a great number of treatments are suggested, few are of value and none specific.

The ideal treatment in cases of hypertrophied prostate is, of course, its radical removal. In the hands of skilful operators the results are excellent. Thus, Judd,² reports a mortality of only 29 (from kidney lesions within two months) out of a total of 542 cases operated on by the Mayos. Young's³ statistics are somewhat better, a mortality of 13 in 400 cases. "During a period of two years and eight months," he writes, "128 consecutive cases were subjected to the operation of conservative perineal prostatectomy without a single fatal result, all of the patients returning to their homes. Forty-three of these cases were over seventy years of age, and 2 were over eighty years of age." Such are the results with selected cases in the hands of our greatest operators. In the ordinary run of cases, however, subjected to the general surgeon, we must expect, as in any other major operation upon elderly people, a high mortality. At least, this is the experience with most of my surgical friends. And what of the inoperable cases? What of those with cardiac, vesical, and renal lesions?

¹ Read at the meeting of the American Röntgen Ray Society, Richmond, Va., September 20, 1911.

² Jour. Amer. Med. Assoc., 1911, lviii, 458.

³ Jour. Amer. Med. Assoc., 1910, liv, 790.

In many cases even when the patient has been subjected to a prostatectomy, nothing has been gained. Thus, to quote Judd:⁴ "The functional result, referring to the power to retain the urine after operation, is almost as important as the question of mortality. We rarely see patients with complete incontinence, and consequently obliged to wear a urinal, who can be kept at all comfortable, and many times they are much worse off than they were previous to the operation." And again: "If a catheter be introduced into the bladder and but a slight amount of residual urine is found in a case having marked secondary symptoms without great difficulty in voiding, we may expect little or no benefit from a prostatectomy, no matter how great the tumor's size. . . . We would operate with great risk." This is the testimony of one of our greatest surgeons. If now we add the fact that 34 per cent. of men, aged over sixty years, are affected with genuine hypertrophy of the prostate,⁵ and that an exceedingly large number of prostatitics are unfavorable for operation, we must see that in the great majority of cases other means must be tried.

With this in view many of our genito-urinary surgeons have sought means less violent or more or less indirect. Bottini attempted to construct a new canal through the prostate by means of the electric cautery. His operation has, however, been only a partial success. The danger of infection, and the formation of scar tissue, must be reckoned with. Upon the assumption that a double oöphrectomy will cause a diminution in the size of a fibroid uterus, the mutilating operation of castration came into favor. But again success was only partial; likewise, the operation of vasectomy. Nor has medical treatment been of any avail. However valuable as an adjuvant, it cannot remove the cause. In most cases, therefore, prostatic massage through the rectum and the intelligent use of the catheter would seem to be the only remedies.

This same massage is useless if employed upon a sclerosed prostate. At best it can only express the secretion from the gland. The kindly forces of nature may then bring about a reduction in size, but it is more probable that the gland will again expand. What we must seek is a method which will at the same time change the internal structure of the gland. We must limit the growth of the soft prostates; we must soften and reduce the harder ones. Such is the task before us. I know of no agent capable of this save the Röntgen rays, and though they have their limitations, as we shall presently see, it will be my purpose to discuss the possibilities of this new form of treatment.

If we review the histology of the prostate,⁶ we find that, unlike most glands, it is surrounded by a capsule made up of non-striated

⁴ Loc. cit.

⁵ Thompson and Guyon, quoted by Judd.

⁶ Böhn, Davidoff, Huber, Text-book of Histology, 1900, pp. 330 to 332.

muscle fibers and yellow elastic fibers. Processes extend inward, thereby breaking up the structure into a number of alveoli. These latter are lined with simple columnar epithelium and contain within the lumen several bodies known as corpora amylacea. When hypertrophy occurs⁷ we are dealing essentially with a hyperplasia, chiefly in the epithelial elements, these latter being thrown into folds.⁸ In order to accommodate this increase in glandular area, we must also have an increase in the muscle and fibrous tissue. In other words, we are dealing with a condition similar to that found in exophthalmic goitre. And, as the Röntgen rays act mostly upon the epithelium, and especially upon that composing glandular tissue, we may expect a rapid decrease in size. But, on the other hand, if there has been a great increase in the muscle or fibrous tissue, the decrease will be but slight. Hence it is that the first and second degrees of prostatic hypertrophy are most amenable to treatment. If we could only know the microscopic appearance of the gland with which we are dealing, our statistics could, through a careful selection of cases, equal those of any operation.

This line of reasoning has been amply borne out by clinical observation. Thus, Robarts,⁹ of St. Louis, reported, in 1902, an improvement in 3 cases of enlarged prostate treated by the Röntgen rays, though he was unable to obtain a radical cure. He came upon this form of treatment by accident and claimed priority. Gautier,¹⁰ during the same year, reported a great relief of the symptoms in these cases, with a diminution of the residual urine. "Decided results," he says, "were obtained in from four to eight sittings." Three years later, in 1905, Carabelli and Luraschi,¹¹ after waiting a year, reported 2 cases, 1 aged sixty-six years and the other aged sixty-five years, completely cured. In the latter the prostate was greatly enlarged and hard, and the residual urine was reduced from 200 c.c. (f5vij) to 10 c.c. (f3iüss). Rollins,¹² of Boston, though reporting no cases, suggested a new technique.

Again, in 1905, Moszkowicz¹³ reported 3 cases, aged, respectively, sixty-one, sixty-six, and seventy-seven years, all of whom had to lead a catheter life. On the day following the first sittings the patients could urinate without the use of the catheter; a week later the prostate was softer, and continued to decrease in size. But in the first case, seventeen days after the last irradiation, there was an epididymitis; in the second, fourteen days after, there were symptoms of a hemorrhagic cystitis. Consequently, the third case was treated only once. A little later he, in company with Drag-

⁷ Ziegler, Text-book of Special Pathology, American edition, pp. 104, 105.

⁸ Ibid.

⁹ Amer. Jour. Derm. and Genito-urinary Diseases, vol. vi, p. 93.

¹⁰ Giornale di Electriana Medica, 1902, iii, 224, and Brazil Medico, 1902, xvi, 403.

¹¹ Gazzetta degl. Ospedali, abstracted in the Jour. Amer. Med. Assoc., September 2, 1905.

¹² Boston Med. and Surg. Jour., 1905, cliii, 153.

¹³ Münch. med. Woch., 1905, liii, 730.

mann,¹⁴ gives his experience with 6 cases, ranging in age from sixty-one to seventy-four years, in which 5 were relieved, and of these, 4 were symptomatically cured.

Tansard and Fleig¹⁵ treated 2 cases. The first was that of a man, aged sixty-three years, who had had two attacks of gonorrhea and one of double orchitis. He was treated nine months and dismissed as cured. The second case, though irradiated only four times, was greatly benefited, though a malignant invasion of the intestinal tract prevented further sittings. Lasseuer,¹⁶ of Lausanne, cites 3 cases, aged sixty-six, sixty-eight, and seventy-two years, who were so greatly benefited that they considered themselves cured, although he had regarded one of them as unfavorable for radiotherapy and advised an operation, which was refused. Tousey,¹⁷ reports that "he has treated several cases, and in some a few x-ray treatments have produced a marked reduction in the amount of residual urine and a return of the ability to urinate without a catheter." In a later communication¹⁸ he reports 1 case treated by the Röntgen rays in conjunction with the high frequency electrode as practically cured. To these, Schlagintweit¹⁹ adds that he has irradiated 53 cases, of whom, 30 received more than three sittings. All of these 30, he says, were greatly improved, although in his experience the residual urine did not decrease in proportion to the other improvement.

On the other hand, Bangs²⁰ doubts the efficiency of the Röntgen-ray treatment as applied to enlarged prostate, and advises the profession to be skeptical of the so-called cures of this condition. He cites a case in which the patient, after treatment with the Röntgen rays, considered himself as cured. But a year later his symptoms recurred, and although he was again treated, he experienced little if any relief. Bangs saw him a little later. The examination at that time, showed an enlarged prostate. Bangs doubts if any real good was accomplished by the Röntgen rays, and thinks that the improvement in the patient was due to the improved hygiene with which he had been surrounded, that is, a Mediterranean voyage, a warmer climate, etc. Consequently, he advises prostatectomy as the only rational method of dealing with these cases.

My own experience has been as follows:

CASE I.—Mr. G., a carpenter, aged eighty years, a widower. He suffered with a gastric hyperacidity and chronic cystitis of eight years' duration. The urine showed a large amount of pus,

¹⁴ Münch. med. Woch., vol. ii, p. 1390.

¹⁵ Ann. des Mal. des org. gén.-urin., Paris, 1906, xxiv, 184, and Fleig, Revue Prat. des Mal. des org. gén.-urin., 1907-08, lv, 203.

¹⁶ Archives d'Electricité Médicale Experimentale et Clinique, 1907, xv, 371.

¹⁷ Med. Elec. and Röntgen Rays, 1910, p. 999.

¹⁸ Amer. Quart. of Röntgenology, vol. iii, p. 143.

¹⁹ Ztsch. f. Urologie, Band i, Nr. 1, pp. 51 to 33.

²⁰ Med. Rec., 1907, lxxi. 902.

but no involvement of the kidney, though when a young man a calculus had been passed. Other history negative. In December, 1906, he exerted himself too severely while at work, and as a result had a severe orchitis. This yielded to treatment, but on February 2, 1907, there was a beginning of prostatic symptoms, among others a frequency of urination (arising as many as six times a night), with pain and burning about two inches from the end of the penis. In spite of treatment, however, the patient grew gradually worse until April 15, when he was able to void only about one-half an ounce of urine at a time. There was also a marked phosphaturia and about 60 c.e. (f5ij) of residual urine.

The Röntgen rays were employed as follows: May 2, 1907, first exposure; May 8, second exposure; May 27, third exposure.

Internal medication was then stopped, and the patient enjoyed complete comfort until June 27, when the entire train of symptoms returned in a much aggravated form.

July 6. Fourth exposure. Some relief, but a slight toxemia occurred as a delirium.

July 16. Fifth exposure. Improvement continued, although slight delirium still occurred. Retained urine as long as two hours at a time.

July 22. Sixth exposure. Improvement continued; voided urine with little trouble.

July 31. Seventh exposure. Retained urine as long as normal; only rose once or twice at night. Felt as well as he ever did and passed a large stream.

August 12. Eighth exposure.

August 25. Ninth exposure. Patient was symptomatically well. No untoward symptoms. Rectal examination revealed a prostate only moderately enlarged. The residual urine had been reduced to 15 c.c. (f3ss).

September 8. Tenth exposure.

October 29. Eleventh exposure. The residual urine had been reduced to 8 c.c. (f3ij).

No further exposures were given, nor was any further trouble experienced until the middle of June, 1908, when the patient had a severe diarrhea with considerable straining at stool. This frequency of defecation, together with old age and an increasing weakness, caused a return of the prostatic symptoms. He voided every half-hour during the day, arose six to eight times at night, suffered severe pain in bladder and penis, and went to bed.

June 29, 1908: Twelfth exposure.

July 1. Thirteenth exposure.

July 3. Fourteenth exposure. Slight relief.

July 12. Fifteenth exposure. A great improvement. Patient rested better, did not arise more than three times at night and required less anodyne.

July 25. Sixteenth exposure. Save for an extreme weakness and a large amount of urination in the early morning, the patient was symptomatically well.

August 1. Seventeenth exposure.

August 19. Eighteenth exposure. The patient arose only once or twice at night and was gaining in weight.

September 18. Nineteenth exposure. The residual urine varied from 8 c.c. (f3ij) to 17 c.c. (f5ss +). Patient remained well.

From this time until his death from cerebral hemorrhage in January, 1909, he remained entirely free from prostatic difficulties. This case, though reported in part on two previous occasions,²¹ is of such interest that I have here reported it in full.

CASE II.—Professor A. L. S., French teacher, aged eighty-four years, married, no children. He had suffered with enlarged prostate for many years, had had several acute attacks, and was obliged to use the catheter. His general health, however, was excellent. There were no urinary complications, probably on account of his having taken large amounts of hexamethylenamine. When first seen, on June 16, 1909, there was a very large and very hard prostate with about 32 c.c. (f5j) of residual urine, also an old intertrigo involving the inner thighs and part of the scrotum.

The first exposure to the Röntgen rays was made on June 16, the second exposure on June 18. Prostate somewhat smaller. Residual urine reduced to 20 c.c. (f3vss); June 19, third exposure; June 21, fourth exposure; June 24, fifth exposure.

About this time, as there was considerable dermatitis, with an exaggeration of the intertrigo, the patient was advised to wait before further exposures were made. On account of the hot weather, he decided to return in the fall. But this he failed to do, and although I have heard from him occasionally, I think that the permanent benefit was only slight.

CASE III.—Referred by Dr. R. S. Spilman and treated in conjunction with him. Dr. C., physician, aged seventy years, married, two children. Five years ago he consulted a surgeon in Cincinnati and requested a prostatectomy, but on account of his poor condition this had been refused. At that time he was treated by intravesical irrigations of boric acid solution with considerable benefit, but during the last year his condition had rapidly become worse; he had had several chills. When first seen on December 11, 1909, there was continual passage of urine and feces with pain and great tenesmus, a very large and hard prostate, some hemorrhoids, and large, congested testicles. His condition was exceedingly poor. The residual urine equalled about 450 c.c. (f5xv), and was of a milky color; about one-half was sediment, pure pus. In other words, the patient when seen was moribund.

²¹ AMER. JOUR. MED. SCI., January, 1908, and Old Dominion Jour. Med. and Surg., January, 1909.

His treatment was as follows: December 11, 1909, first exposure; December 14, second exposure; December 16, third exposure; December 18, fourth exposure; patient retained urine one hour. December 20, fifth exposure; retained urine one and one-half hours. December 22, sixth exposure; retained urine two hours, and there was less tenesmus. December 24, seventh exposure; condition about the same. Prostate somewhat smaller and harder. December 27, eighth exposure; felt much better, although he retained urine only about one hour. Hemorrhoids much better, testicles normal in size.

From this time until January 27, 1910, no exposures were given, though the bladder was irrigated and hexamethylenamine administered. The residual urine varied from 375 c.c. (f5xiiss), to 600 c.c. (f5xx).

On January 27 the tenth exposure was given; February 2, eleventh exposure; February 16, twelfth exposure; February 26, thirteenth exposure.

There was little further improvement, though the residual urine was reduced to about 135 c.c. (f5ivss). His death from pyonephrosis occurred about four weeks later.

CASE IV.—Referred by Dr. H. M. Nash. Judge S., lawyer, aged sixty-eight years, married, one child. He had been suffering six months with prostatic symptoms, which had gradually been getting worse. He arose two or three times at night, and has had to use a catheter on several occasions. When first seen, on February 12, 1910, the prostate was moderately enlarged and fairly hard. Urine normal. As the patient requested that no catheter be passed into his bladder, I am unable to give the amount of the residual urine.

The exposures were made as follows: February 12, 1910, first exposure; February 14, second exposure; patient felt better. February 16, third exposure; patient urinated as well as he ever did. February 18, fourth exposure; February 21, fifth exposure; patient felt much better. February 23, sixth exposure; February 25, seventh exposure; February 28, eighth exposure; March 3, ninth exposure. Patient was now able to rest the entire night. Urination normal.

A second series of exposures for prophylaxis were given as follows: April 7, tenth exposure; April 11, eleventh exposure; April 14, twelfth exposure; April 17, thirteenth exposure; April 21, fourteenth exposure; April 25, fifteenth exposure; April 28, sixteenth exposure; May 2, seventeenth exposure; May 5, eighteenth exposure. Prostate reduced in size and soft.

From April 11 to June 10, prostatic massage was also given, with the result that the patient continued to improve, slept the entire night, with no pain upon urination, and there was practically a disappearance of the prostatic enlargement. He complained,

however, of a slight irritation of the deep urethra, which was promptly relieved by the passage of a sound.

From this time until July 1, 1911, he remained free from prostatic symptoms. On that day I was again consulted, and found his prostate somewhat enlarged. It was massaged. This was also done on July 21. Röntgen-ray exposures were given on August 2 and 6. All of the symptoms have disappeared and the patient remains well.

Perhaps in the light of this case we can understand Bangs' somewhat contradictory statements.

CASE V.—Mr. A., merchant, aged sixty-eight years, married, three children. He had had prostatic symptoms for about two years. A few months before he had had a severe orchitis, resulting from some heavy lifting. He arose four or five times at night; urinated about every hour and a half during the day; had hemorrhoids and some tenesmus, and his sleep was disturbed. First seen on October 24, 1910, when an examination showed a rather large and moderately hard prostate, with a residual urine of 25 c.c. (f3vj). The urine was cloudy and contained pus, but no casts. Pulse tension equalled 140 mm. of mercury.

October 24, 1910, first exposure given; October 25, second exposure; October 27, third exposure; October 31, fourth exposure; November 2, fifth exposure. Prostate slightly smaller. Residual urine, 20 c.c. (f3vss). November 5, sixth exposure; November 8, seventh exposure; November 12, eighth exposure; November 17, ninth exposure. Residual urine still 20 c.c. (f3vss). November 25, tenth exposure. Sleeps from three to four hours between urinations.

During this series of exposures the bladder was also irrigated and the prostate massaged, while hexamethylenamine and boric acid were internally administered. The residual urine varied from 20 c.c. (f3vss) to 50 c.c. (f3iss+). On December 9 the residual urine was 23 c.c. (f3vj), while he slept the night before as long as four and one-half hours between urinations. On December 24 he arose only twice during the night, while during the day he went as long as four or five hours between urinations.

Röntgen-ray treatments were resumed as follows: December 26, eleventh exposure; residual urine, 14 c.c. (f3iv). December 27, twelfth exposure; December 31, thirteenth exposure.

The irrigations were continued, and on January 7 the residual urine was 8 c.c. (f3ij). But from January 13 to February 5 he was confined to bed by a blistered perineum, brought on by his own application of hot compresses in the hopes of easing hemorrhoids. The healing, however, was complete. Irrigation of the bladder and massage of the prostate were again begun, with the use of sounds and some applications of argyrol to the deep urethra. When last seen on April 8, 1911, his urine was still cloudy; he

arose only once, or at most twice, at night, went about four hours between urinations during the day, and slept well. His prostate showed only a very slight enlargement and the testicles were normal in size. In short, save for the cloudy urine, he appeared symptomatically well.

He was, however, not entirely satisfied, and consulted an eminent genito-urinary surgeon in a neighboring city. I have since learned that a papilloma was removed from the bladder and the remaining prostate through a suprapubic opening.

CASE VI.—Dr. E., dentist, aged fifty-eight years, married, three children. He had been complaining for several months of prostatic symptoms gradually becoming worse. Urinated every half-hour, day and night, with great pain and tenesmus; had been treated by a New York electrotherapist with a high-frequency rectal electrode without avail. He was rapidly becoming worse. First seen December 6, 1910. At that time I found a large soft prostate and a strictured urethra. The urine was phosphatic and contained pus. Operation was advised for the stricture, but refused.

The following Röntgen-ray treatments were then given: December 6, 1910, first exposure; December 7, second exposure; December 8, third exposure; December 10, fourth exposure; December 14, fifth exposure. No relief. An attempt was made to pass a sound in the office, but it was not successful. An operation was again advised, and this time accepted.

December 23, operation, St. Vincent's Hospital. I did a forceful dilatation of the urethra under anesthesia up to a 29 F. sound. Even then, strange as it may appear, I was unable to catheterize him. That afternoon he emptied his bladder unassisted, the first time in many months. A rectal examination made at the time of the operation showed the prostatic tumor almost gone.

Further Röntgen-ray treatments were given on January 4, 1911, sixth exposure, and on January 26, seventh exposure. Treatment by sounds has been continued. Prostatic symptoms have entirely vanished.

When last seen on May 27, 1911, the patient was advised to continue passing the sounds. His urine, though still very bad, was gradually improving under the use of antiseptics. With the exception of an occasional tenesmus, the old symptoms had entirely vanished.

Of course, in this case it was the dilatation of the urethra that brought about the greatest relief, but to the application of the Röntgen rays must be ascribed the disappearance of the prostatic tumor.

CASE VII.—Judge E., merchant, aged seventy-six years, widower, three children. For three or four years he had been suffering with prostatic symptoms, and arose every two hours during the night.

First seen April 4, 1911. Examination showed a prostate slightly enlarged and soft. Urine normal. Residual urine, 27 c.c. (f3vij).

April 4, 1911, first exposure made; April 6, second exposure; April 8, third exposure, improvement; April 11, fourth exposure. Arises only twice during the night and considers himself much better.

Further exposures were then discontinued on account of the patient going on a business trip. When seen on May 18, he was advised, on account of the hot weather, to discontinue the treatment until the fall. When seen July 11, he reported a continuous improvement.

The technique in the treatment of hypertrophied prostate is largely one of individual preference. It is a question of position and dosage. Thus, Robarts treated his cases while seated upon a chair, there being a window in the seat exposing the perineum. The tube was placed below. Gautier irradiated both perineum and lower abdomen. Carabelli and Luraschi placed their patients upon an inclined plane. Tansard and Fleig used a specially constructed diaphragm. Lasseuer and myself prefer a Sims' position. Lasseuer first irradiates the prostate at right angles to the line of its axis; later, directly upon the perineum. My own cases have been treated in the latter way. Moszkowicz and Schlagintweit employed a rectal speculum, but this feature of their technique has been greatly condemned.

Many of the operators have advised the protection of the testicles by lead foil. They claim that the danger of sterility is thus avoided. In my own series of cases I have found in almost all an abnormal increase in the size of the testicles, most of which, in my opinion, has been due to the congestion resulting from straining. So I have also irradiated the scrotum in all cases save one. I have found great relief and, further, a return to the normal size. As what we wish is a reduction of the prostatic symptoms, and a double castration has often accomplished this end, I am of the opinion that the irradiation of the scrotum is a thing eminently to be desired. Of course, we are now speaking of the prostatic hypertrophy of elderly men. We are not discussing these enlargements in younger subjects due to a gonorrheal infection.

The question of dosage is most important. Many operators have prescribed specific amounts. Thus, Tansard and Fleig prescribed 5 Holznecht units during the first series of irradiations, and another 5 Holznecht during the second. All prefer moderately high and well-seasoned tubes. Tansard and Fleig specify a No. 7 on the Benoist radiochronometer. Schlagintweit, a No. 7 on the Wehnelt scale. Personally, my work has all been done with coils, of which I have had three, one of 12 inch spark length, and two of 18 inches. I have also used both mercury and Wehnelt interrupters. My present technique follows that used in the treat-

ment of skin affections, save that the tube must be hard and well seasoned. I try to place three or four layers of the primary of the coil in series and to use from four to six ampères of current with a Wehnelt interrupter; that is, from one and one-half to two milliampères in the secondary circuit. Exposures of from five to ten minutes are given at frequent intervals and until a moderate dermatitis has resulted. Sometimes I employ the leather filter. There is one thing upon which I do insist. The full physiological dosage must be given. And this varies in different individuals.

Thus we see that the treatment of hypertrophied prostate by the Röntgen rays is closely akin to that used in exophthalmic goitre. It is largely a question of the histological structure of the gland. If the growth is young, and consequently a hyperplasia due to the increase of epithelial and glandular tissue, we may expect brilliant results. On the contrary, if there has been much increase of the muscular or fibrous tissue, it is only by the greater contraction of this tissue that relief can be accomplished. Massage is indicated as an adjuvant in these cases. In the third degree but little benefit may be expected. Aside from the relief of the localized congestion, there will be no improvement in the symptoms. Muscle tissue and old fibrous tissue will not yield to the Röntgen rays.

To conclude: We have in the Röntgen rays a valuable treatment in cases of hypertrophied prostate. As there is no question of mortality, all sufferers may be subjected to its influence. If there is to be an improvement, it will be rapid. If no improvement occurs in a reasonable time, other treatment must be considered.

CANCER OF THE OVARY IN A GIRL, AGED ELEVEN YEARS.

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THE occurrence of cancer of the ovary at the age of eleven years, the misleading symptoms, the fact that a complete autopsy was done, and the material worked up thoroughly, makes this, the writers believe, a case well worth reporting.

The history of this patient is as follows: Miss B., aged eleven years, schoolgirl. The family history is unimportant.

Past History. Four months ago she was operated upon in another state for appendicitis. (No pathological report.) The appendix was removed and several small cysts in both ovaries punctured. From this operation the patient made an uneventful recovery, so far as healing of the wound was concerned, but she did not regain her strength. Soon she began to lose weight and ran an irregular temperature. She became pale and pasty in appearance, and spent most of her time in bed, complaining at times of pain in her lower abdomen over both sides.

Present Illness. Six weeks later one of us saw the patient on account of her right knee, which was swollen, somewhat hot, full of fluid, and quite tender—so much so that she could not walk upon it. No other parts being involved, a supporting bandage, ham splint, and rest in bed were advised, and under this treatment her family physician reported that the swelling soon reduced and the pain disappeared.

Six weeks later she was again seen on account of vomiting of several days' duration, increasing emaciation, and general enlargement of the abdomen. She was found much more emaciated, complaining of almost constant epigastric pain, vomiting nearly everything taken, and her abdomen was tensely distended by fluid. On palpation, it was possible to make out a hard irregular tumor in her epigastrium, about the size of a large grape fruit. On vaginal examination little could be gained, as the tense abdominal wall, small vagina and hymen prevented satisfactory palpation. The temperature had been irregularly elevated, but was never over 100.4° in the evening. The leukocytes were 10,800. The urinary findings were negative.

An operation was advised, as it seemed likely that the condition might be tuberculous peritonitis, possibly overlooked at the operation for appendicitis.

Operation. A median incision was made between the umbilicus and pubis, and a large amount of cloudy fluid let out of the abdomen. The hand was then inserted, and everywhere large nodular masses were found.

About the stomach there was a large mass running parallel with the transverse colon. Both ovaries were about equally enlarged, being two or three times their normal size. Their surfaces were symmetrically studded over with nodules, each about the size of a small English walnut. The ovaries themselves were hard, solid, and of abnormal consistency. The pelvis was filled on all sides by a hard nodular growth. Numerous nodules were felt along the root of the mesentery of the small intestine, and everywhere the bowel was bound down by adhesions to these masses. The cecum was examined for the appendiceal stump, but none could be found, as it had been inverted.

After this hasty examination it was at once evident that the

condition was hopeless, and not to be improved by further operation. The right ovary was freed, its vessel ligated, and the organ removed for pathological examination. The abdomen was then hastily sutured, and the patient returned to bed.

Following the operation the abdomen again filled up with fluid, vomiting continued, and the patient gradually failed until the twenty-eighth day, when she died. An autopsy was performed by one of us (Dr. S. R. Haythorn), then of Harvard Medical School Pathological Department, and the report of the presence of an adenocarcinoma and the pathological findings, together with photomicrographs of the tumor, are submitted below.

This case was misleading in that four months before, the abdomen had been opened, its contents explored, and the appendix removed. At that time both ovaries were pulled into the wound to puncture cysts, so that their consistency and size were necessarily noted. The gradual decline, the accumulation of fluid, and the occurrence of an effusion in the knee-joint naturally inclined one toward the diagnosis of tuberculous peritonitis, possibly overlooked during the operation for appendicitis. The rarity of carcinoma at such an age, and the rapid development of all symptoms directly after operation, made the case almost, it seems to the writers, an impossible one to diagnosticate. Had there been less fluid in the abdomen, and had the vagina been larger and without a hymen, evidence might have been obtained from which correct conclusions might have been drawn.

It would seem from the autopsy findings, carcinoma not having been discovered elsewhere than in the ovaries and lymphatics, that there can be only two hypotheses as to its occurrence: (1) A secondary implantation of cells from a carcinomatous appendix directly into the ovaries; and (2) the primary development of carcinoma in the ovary itself, with metastasis into the opposite ovary.

In favor of the first theory is the occurrence of symptoms of appendicitis. Many of the cases of cancer of the appendix have been in young children, and have been operated upon with a diagnosis of appendicitis. One of the writers has observed such a case with typical symptoms of chronic appendicitis. Additional evidence in favor of secondary implantation is the equality in the size of both ovaries and the symmetrical arrangement of nodules in each; the preparation of the ovaries to receive implantations by puncturing of cysts; and the crushing of both tip and base of appendix in its removal, which is known to have been done.

In support of the second theory is the well-known fact that cancer is sometimes primary in the ovary, particularly in young girls, and that it frequently metastasizes into the opposite ovary. Here it must be said that at least some inequality in size between the primary and secondary growth would be expected; although

this is not necessarily true, since elsewhere in the body it has frequently been proved that metastases may outstrip primary growths. The most conclusive evidence in favor of the second explanation is the finding of tumor cells in the ovaries that exactly correspond to the cells found in the metastatic growths. Here we have no supposition, but a fact, and beyond this we can only conjecture.

In going over the literature, it is evident that carcinoma of the ovary in children is very uncommon, but not a rarity. Numerous cases are reported, some of which are carcinomatous degeneration in mixed tumors, others cancerous degeneration of cysts, and others primary carcinoma developing in the ovary itself. Many of the recorded cases are unaccompanied by pathological reports, or at best have only meagre ones, making it almost impossible to group them so that they are of any value. From the writings of others, many points which have been of interest to the writers, may also prove so to others who have not had occasion to go over the literature on this subject.

Many of the cases reported have been operated upon, as was this one, with a diagnosis of tuberculous peritonitis, principally on account of the presence of fluid in the abdomen without anasarca. This has been the most constant sign in the recorded cases, not more than 2 or 3 cases having been reported without it. Other signs which should make one suspicious of malignancy are: Pain, rapid emaciation, cachexia, cessation of menses, and edema of the extremities; particularly bilateral tumors; also hard and knotty ones of rapid growth, and proof of metastasis (Baader¹). Another condition spoken of by reporters of ovarian tumors in children is the occurrence of early puberty, said sometimes to disappear after the tumor has been removed.

The diagnosis between carcinoma and sarcoma must only rarely be possible. Certain distinguishing signs are pointed out by Berent,² however. It is said that sarcoma is almost always primary, and if secondary, is, as a rule, from a uterine tumor, while cancer metastases in the ovaries, even from distant foci, such as stomach and breast, are not at all uncommon. Sarcomas are also said to metastasize and form adhesions later than carcinomas. In regard to size, sarcomas are apt to become much larger than carcinomas. It is also stated that carcinoma in relation to the ovary has a greater preference for young people than sarcoma. This we believe to be doubtful, in view of the number of cases of sarcoma of the ovary reported in young people. Pfannenstiel reports that in a large series the average age for the occurrence of sarcoma of the ovary was thirty-two years, with 40 per cent. in individuals under twenty-five years of age.

¹ Ein Fall von Carcinom des Ovarium im jugendlichen Alter, Tübingen, 1895.

² Ueber Maligne Ovarialgeschwülste bei Kindern, Berlin, 1901.

It may, therefore, be concluded, that:

1. The accurate diagnosis of malignant tumors of the ovary in young girls seems rarely possible.
2. Fluid in the abdomen in children without general anasarca, provided adhesive pericarditis and cirrhosis of the liver may be ruled out, should always be investigated by exploratory laparotomy.
3. Ovarian tumors, particularly in young girls, should be removed with the least possible delay.
4. The occurrence of metastatic nodules in the fossa of Douglas, or in any other location where they may be definitely made out, should be accepted as evidence of extension too great to permit the case to be benefited by operation.

The pathological findings in the ovary that was removed at the operation, as well as a synopsis of the autopsy protocol of this case, are as follows:

SURGICAL SPECIMEN FROM OVARY (Harvard, 1909, No. 766). *Microscopic Description.* The sections were of a rapidly growing medullary tumor, the cells of which varied considerably in size, but were similar in structure. The average cell was twice the diameter of a polynuclear leukocyte. The next most common cell was again as large, and usually possessed from two to four nuclei. A third type of cell was a little larger than a large lymphocyte. The cells were round, oval, indented or elongated, depending upon the compactness of the surrounding growth. There was constantly a wide margin of clear protoplasm about the one or more nuclei, which were globular in outline and slightly vacuolated, giving them a cart-wheel appearance. The nuclei stained deeply and were usually multiple. Occasional monasters and diasters were present. The cells were held in cords or nests by a fine, fibrous reticulum, to which they did not appear to be attached. A general parallel arrangement of these columns of cells was preserved. The connective tissue stroma was gathered together into bands which ran either to a thin capsule or to a central connective mass. The bloodvessels were found only in the connective-tissue strands. Lymph spaces filled with free tumor cells were seen. There was practically no inflammatory reaction present. Diagnosis: Solidly growing carcinoma of ovary.³

ANATOMICAL DIAGNOSIS FROM AUTOPSY PROTOCOL. Carcinoma (primary in ovaries). General metastasis of lymphatic distribution occurring in ovaries, uterus, pleura, peritoneum, esophagus, stomach, small intestine, colon, pancreas, gall-bladder, adrenals, urinary bladder, diaphragm, abdominal muscle, skin, mammary glands, and peribronchial, cervical, axillary inguinal, mesenteric, and retroperitoneal lymph nodes.

³ We wish to express our thanks to Dr. F. B. Mallory and to Dr. Oskar Klotz for their opinions as to the nature of this tumor, and as to its probable primary site.

Other conditions present but not described below were: Atelectasis of lungs, ascites, hydrothorax (double), hydropericardium, edema of the left leg and two healed operation wounds on the abdomen. The absence of secondaries in the organs, namely, heart, lungs, spleen, liver, and kidneys, was striking when compared to the extensive distribution throughout all the lymphoid structures examined.

Synopsis of Autopsy Protocol. The body was greatly emaciated, development slight. Cervical, axillary, and inguinal nodes greatly enlarged, firm, and infiltrated. The left inguinal nodes were enlarged and adherent in a mass over the region of the inguinal ring, causing compression of the femoral vein and edema of the left leg. Nodular extensions upward from this mass infiltrated the whole of the left lower quadrant of the skin and abdomen. Both breasts were enlarged and nodular in contour. The umbilicus protruded slightly. Two healed operation scars were seen on the abdomen—one in the appendix region and the other, 10 cm. long, was 4 cm. to the right of the median line to which it ran parallel.

Pleural cavities: Both pleural cavities contained several hundred cubic centimeters of turbid yellow fluid. On the left there was so great an amount as to completely compress the lung. On the sternum, the upper surface of the diaphragm, and the parietal pleura were numerous spheroidal nodules, white in color and firm in consistency, which extended out into the pleural cavities. The visceral pleurae were marked by white cord-like lines, having occasional small white bodies situated upon them. These bodies varied in size from small spots to nodules 1.5 cm. in diameter. Two large ones upon the left side were pedunculated.

Left lung: The nodules were most numerous between the lobes. The lung was collapsed, atelectatic, firm in consistency, and dark reddish gray in color.

Right lung: The right lung was larger than the left and was air-containing throughout. The peribronchial lymph nodes were enlarged, several measured 3 cm. in diameter. They were milk white in color, and of moderately firm consistency.

Pericardium and heart showed no tumor.

Peritoneal cavity: A large, white, friable mass, 5 cm. in diameter, lying in the rectus muscle, was bisected by the incision. The breasts contained many similar masses. A large washbowl full of fluid was removed from the abdominal cavity. The parietal peritoneum was studded with innumerable small, white, solid nodules. There was a large chain of closely approximated, encapsulated nodules averaging about 3 cm. in diameter, extending across the omentum between the stomach and the transverse colon. The omentum was free from fat; it contained several small sacs filled with straw-colored fluid. The small intestines were held firmly in place by the mesentery, between the layers of which were great

masses of nodules, many of them 5 and 7 cm. in diameter. The cecum, ascending and descending portions of the colon were densely adherent to the parietal walls. The pelvis was so filled with similar masses that relations could not be made out.

Spleen: The spleen was relatively large. A secondary growth, 2.5 cm. in diameter, was situated in the hilum. The capsule and the splenic pulp were otherwise negative.

Gastro-intestinal tract: The esophagus showed a great number of small nodular secondaries beneath the mucosa. The stomach wall was generally thickened and everywhere studded by small submucous nodular secondaries. The small intestine was firmly fixed throughout its entire length by the large secondaries in the mesentery. Its walls were thickly studded with discrete small spheroidal masses, which lay beneath the mucosa, which were not ulcerated, but produced bulgings in the lumen and beneath the serosa. The cecum was firmly embedded in the pelvic mass. The stump of the appendix could not be found. The condition of the colon resembled that in the small intestine. The rectum was inseparably bound in a mass of new growth in the pelvis.

Liver: The liver was negative and no secondaries were found. There were new growths of a nodular type about the gall-bladder, the bile ducts, and in the gall-bladder wall.

Pancreas: The pancreas was irregularly club-shaped, measuring 14 x 7 x 6 cm. The enlargement was due to new growths involving the lymph nodes about the head of the pancreas, and occurring in smaller masses throughout its length. The new growths were from 3 to 6 cm. in diameter, and were apparently separated from the true pancreatic tissue by a thin fibrous membrane.

Kidneys: The upper pole of the left kidney was embedded in the new growth about the adrenal and separated from it by a fibrous membrane. The growth did not invade either kidney. The ureters and pelvis were greatly dilated on account of the pressure of the pelvic tumor constricting the lower ends of the ureters.

Adrenals: About one-half of each adrenal was replaced by a globular new growth. These masses were much softer than those in other parts of the body. The one on the left measured 8 x 5 x 5 cm., and extended downward about the pole of the kidney and rested upon the upper surface of the renal vessels.

Aorta: The aorta was surrounded by masses of lymph nodes containing new growths. The lumen was negative.

Pelvic mass: The pelvis was filled with an adherent, infiltrating, friable tumor mass. A densely adherent, thick-walled cyst was found in the position previously held by the ovary removed at operation. It contained semifluid grayish-red material. The walls measured 2 cm. in thickness, were dark reddish-gray in color, smooth on the inner surface, and friable in consistence. The left ovary was 8 cm. in diameter, firm, hard, and adherent. The

tubes and fundus of the uterus were all bound in an inseparable mass of reddish-gray tumor. This mass was continuous above with the retroperitoneal lymph nodes, and downward with a mass of nodes surrounding the femoral and inguinal rings and vessels.

In taking up the microscopic findings of this case only those points are described which seem to have a more or less direct bearing on the tumor and the distribution of its secondaries. Other conditions which were found are simply mentioned. The microscopic appearances of all the sections which contain new growth are so constant, and so similar to those found in the ovary, removed

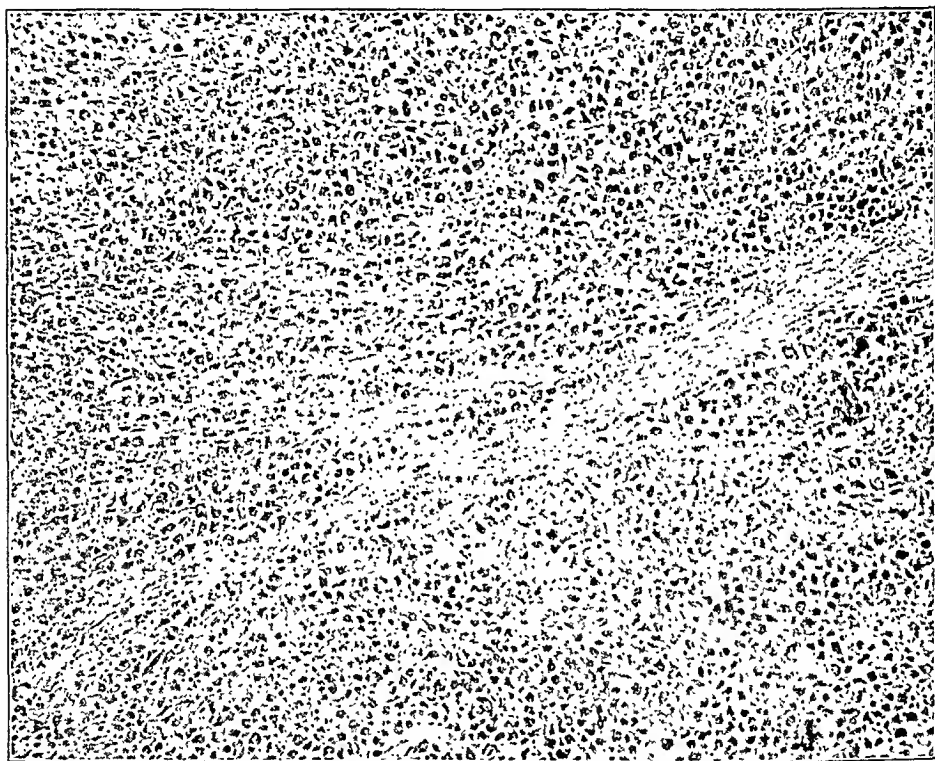


FIG. 1.—Section showing the typical structure of the tumor which was characteristic of the primary and all of the secondary growths. Objective Zeiss AA. Stained with hematoxylin and eosin.

surgically for diagnosis, that further description would cause unnecessary repetition (Fig. 1). The small nodules wherever found look like areas which might have been punched out of the tumor described above. Each one is provided with a very thin fibrous capsule. Hereafter they will be mentioned as secondaries.

Lung: In portions they were completely atelectatic. There was no tumor in the lung proper. Included within some of the lymph spaces of the pleura were typical secondary tumor nodules. In the neighboring lymph spaces and in the lymph spaces of the interlobular septa there were colonies of free tumor cells.

Spleen: The spleen was free from secondaries. The tumor mass at the hilum did not extend through the capsule.

Stomach: Portions of the stomach mucosa were practically normal. These passed gradually into the areas where the crypts had disappeared, and the mucosa had taken on the appearance of the tumor. The surfaces of these areas were necrotic, showed masses of bacteria, and were infiltrated with polymorphonuclear leukocytes. No true ulcers were found. The tumor of the mucosa extended downward to the greatly thickened muscularis mucosa. Numerous secondary tumor nodules were found in the submucosa. The subserous lymph spaces were dilated and filled with free tumor cells. The muscularis showed no secondaries.

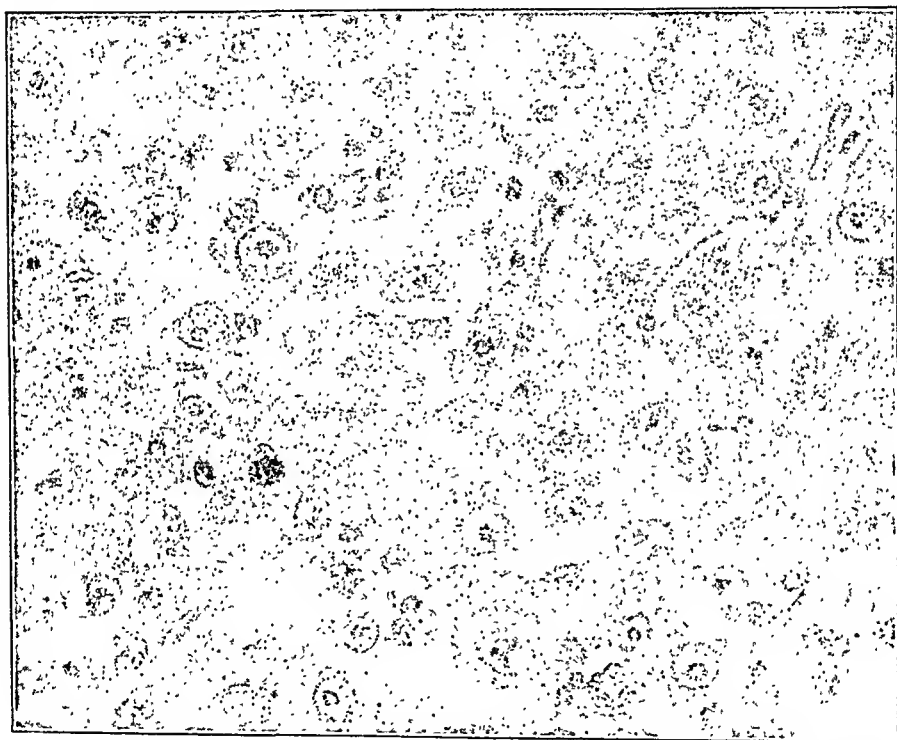


FIG. 2.—A cellular portion of one of the secondaries in the wall of the small intestine. Magnification Zeiss objective DD.

Small intestine: Sections from the upper part of the small intestine showed that the lymphoid tissue had been replaced by tumor tissue, which sometimes appeared as polypoid growths on the sides of the valvulae conniventes. The connective tissue of the valvulae was infiltrated with masses of secondaries. The muscular layers were not affected and served to separate the small submucous nodules from the large tumor masses in the mesentery. Sections from the lower part of the small intestine showed the mucosa had been replaced by ordinary granulation tissue (Fig. 2). There

were numerous discrete secondary nodules in the submucosa. The dilated lymph spaces of the mesentery were filled with free tumor cells. Within several veins there were seen, lying free among the red blood corpuscles, cells which to all appearances were tumor cells. These could easily be distinguished from endothelial cells which had been stripped from the vessel walls. Both types of cells were seen in some of the veins.

Pancreas: The pancreatic tissue appeared normal, and was separated from the tumor by fibrous bands. The secondary nodules in the pancreatic lymphatics showed areas of necrosis, in which the parallel arrangement of the stroma was especially well seen. Veins containing tumor cells were seen here in the borders of the secondaries.

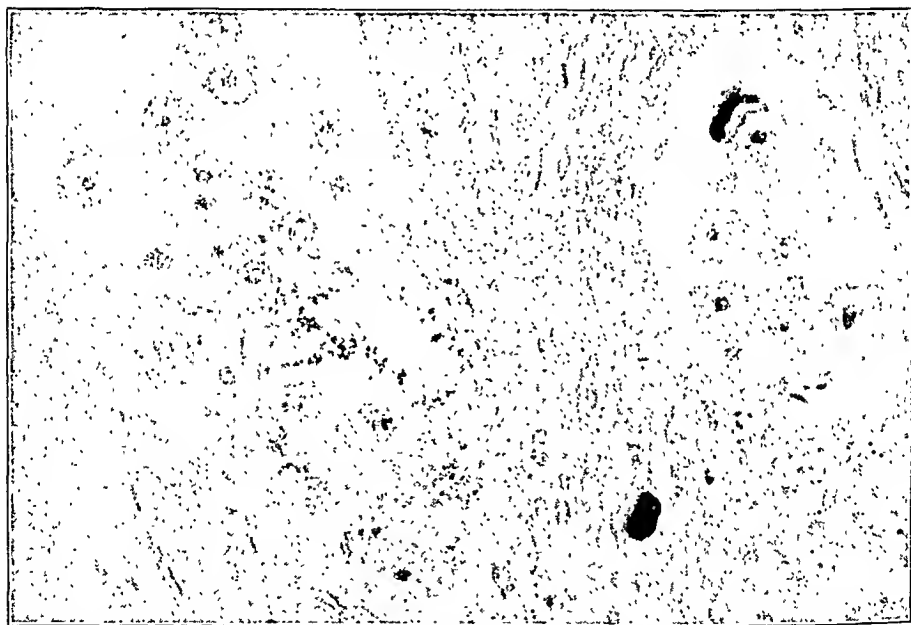


FIG. 3.—Lymph sinuses in the neighborhood of a secondary growth of the mesentery containing free tumor cells. Objective Zeiss DD.

Liver: No secondary growths were found. In the sinusoids and in some of the vessels there were rather numerous large cells. These cells resembled poorly stained tumor cells, were three to five times the diameter of a red corpuscle, had a distinct margin of protoplasm, a poorly stained nucleus, and one or more nucleoli, which were twice the size of the nuclei of the neighboring cells.

Kidneys: There were no secondaries. In some of the veins cells resembling tumor cells were seen. A mass of secondary growth was separated from the kidney by the fibrous capsule.

Adrenals: These showed large nodules of secondary growth.

Pelvic tumor: Sections from the pelvic mass showed the typical

tumor growth. Here the connective tissue reticulum was more pronounced, the multinucleated cells relatively more numerous, and nuclear figures more common.

Summary. To sum up, we have a rapidly growing, malignant tumor, which produced very extensive metastases of lymphatic distribution. The structure was that of an epithelial growth of a round- or oval-celled type, which always reproduced the same picture and never developed cylindrical cells or became scirrhous. These points, added to the fact that the growth was first seen in the ovaries, leads to the supposition that it was primary in one or both of them. Most interesting were the cells in the mesenteric veins and in the

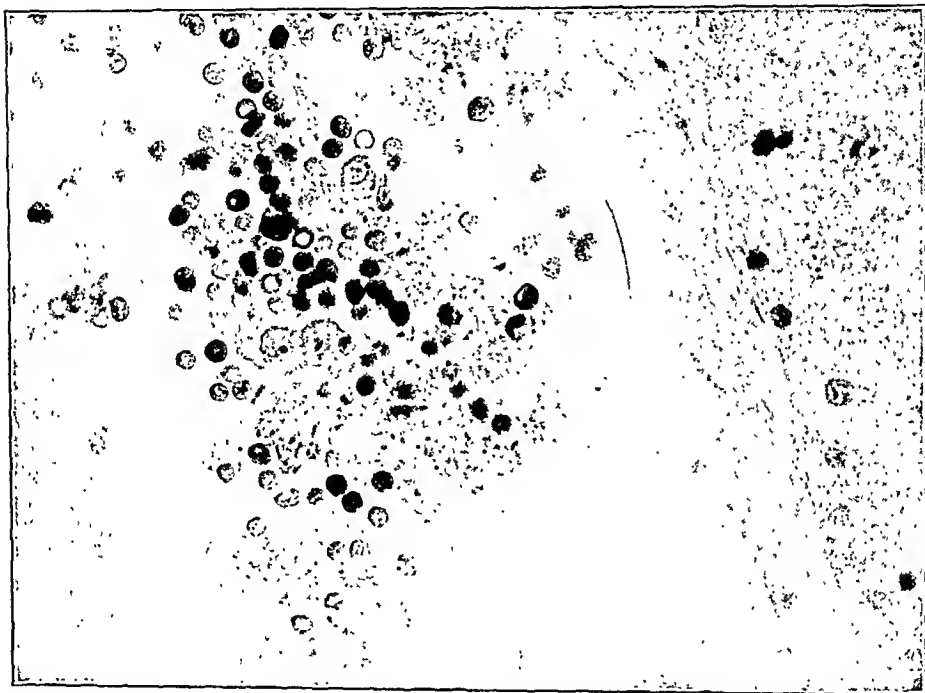


FIG. 4.—Small vein of the mesentery containing free tumor cells Zeiss objective DD. The background immediately around the free tumor cells was slightly retouched.

liver, which appeared to be free tumor cells (Figs. 3 and 4). In the mesenteric veins there seemed to be little doubt that they were tumor cells, for they exactly resembled those in the lymph spaces, had nucleoli, and were larger than desquamated or wandering endothelial cells. In the liver they were not so well stained, but could be differentiated from displaced liver cells, in that they had larger nuclei, and were free from fat globules and pigment granules, while there was abundant pigment in the neighboring liver cells. Those found in the liver sinusoids were distinguished from wandering endothelial cells with difficulty, their greater size being the only obvious point of difference. None of these cells was found in the lung capillaries. The customary teaching on these tumors which metastasize wholly

by the lymphatics is that the cells do not gain entrance to the blood stream; but granting that the cells observed were tumor cells, another explanation must be sought in this case. Three possibilities have suggested themselves: (1) That the blood had closely associated with it (maybe with the red cells) an immune body which brought about the destruction of the tumor cells, but did not diffuse through to the lymph. (2) That the tumor cells were carried to the liver by the portal circulation and destroyed. (3) The most likely possibility of all is that the question was a quantitative one, the lymphatics in the neighborhood of new growth being filled with great numbers of tumor cells, while some search was required to find those in the veins.

PHYSICAL EXERCISE AND BLOOD PRESSURE.¹

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My attention was first called to this subject while making a physical examination of members of a large men's gymnasium. The men were young or middle-aged, with one or two exceptions, and the great majority of them were engaged in indoor sedentary occupations. The exercise was taken as a recreative, hygienic measure, and consisted, for the most part, of the well-known class work, done to music, embracing pulley weights, free hand, dumb-bell, bar-bell, and Indian-club exercises, marching, dancing, deep breathing, and finally, a sharp run; lasting altogether from half to three-quarters of an hour.

It occurred to me that perhaps by means of the systolic blood pressure, taken at three periods, namely, just before, immediately after, and then a little later after a short rest or after the usual bath, I could obtain some definite idea of the effect of the exercise in each individual case, and thus have some practical guide as to the amount and severity of the work best suited to each person. Even the ordinary class work arranged for the average individual might be too severe for some, and, consequently, defeat the purpose for which it was taken as a recreative measure. Of course, I recognized that other elements besides the blood pressure entered into the problem and must be considered, but it seemed to me that the blood pressure might be one test, of a definite character, which would be of practical value in determining the proper kind of

¹ Read before the American Climatological Association at Montreal, June 14, 1911.

exercise and the amount best suited to each person. I accordingly took the maximum blood pressure, at the three periods mentioned, of 59 men, 6 boys, and, through the kind permission of Dr. Sargent, of Cambridge, of 32 young women, pupils in the Sargent Normal School of Physical Education. In addition, I took the blood pressure of the first two periods, just before and immediately after exercise, of 29 men, making, altogether, rather over 350 separate measurements.

I found it no easy matter to make these observations, for my material was not always as tractable as the inert or inarticulate subject of the laboratory. Sometimes after one or two measurements the man would disappear and the observation would be left incomplete. Again, I found more or less difficulty in getting the men before they had taken any exercise; and immediately after exercise a number of men would appear at the same moment for the second measurement, so that the blood pressure of all could not be taken soon enough to make the observation of the most value. I found I could hold the men best by telling them, at the time of the initial measurement, that I could give them no idea as to how their hearts were working until I obtained all three measurements. With the girls it was different, for they were more directly subject to the order of the director of the school, and, in general, they showed rather more intelligent interest.

The measurements were taken with a "Tycos" sphygmomanometer, which I had compared with a mercurial instrument and found to be substantially in agreement with it. I found this instrument exceedingly useful for this work, because the measurements had to be taken rapidly, and this the "Tycos" enabled me to do.

When I began these investigations, I was unaware that so much work had been done upon the effects of muscular effort on blood pressure, both by American and foreign investigators, and I am indebted to my colleague, Prof. Dearborn, for a bibliography upon the subject. Much of the work done by others, however, relates to the effect of severe, extreme exertions upon the blood pressure, while my investigations have to do only with moderate, comparatively mild exercise as illustrated by class work, or with a short, sharp effort, like running up and down stairs, or a few laps on the running track of the gymnasium. In all the investigations, those of my own and others, practically the same results have been obtained as regards the variations of the blood pressure before, during, and after exercise, depending upon the character, length, and intensity of the exercise. In brief, after prolonged and severe exertion there is a diminution of blood pressure from the normal at the conclusion of the effort. Thus, Baldes, Heichelheim, and Metzger² examined 12 young men, aged between seventeen and

² Münch. med. Woch., September, 1906, No. 38, p. 1865.

twenty-seven years, after a forced march of 100 kilometers, and found in all a diminution of blood pressure. Gordon³ took the blood pressure of 2 football players in an international Rugby football match, and found a marked fall in both cases. Potter and Harrington⁴ found that in 10 Marathon runners, all exhibited a low blood pressure after the race except 1, who was the winner, and who had a pressure of 160 after and 120 before. Three were examined before and after another race, and in the examination after the race all showed a blood pressure below 105, while before it had been 140. Barach⁵ found in 55 Marathon race contestants, that the maximum blood pressure before the race was 126.5 (53 cases), and 107.3 (38 cases) after the race. Ten days subsequent to the race the pressure was 124.7 (19 cases). Lowsley,⁶ after a twenty-mile race, found the blood pressure below normal, and his conclusions are that "rapid exercises (vigorous, fatiguing, exhaustive) are followed by a fall of pressure below normal which lasts longer than after moderate exercise, even if the former is continued for a very short period and the latter for quite a long period of time; furthermore, the return to the normal pressure after the subnormal phase is slower the more exhaustive the exercise."

On the contrary, after a short period of mild or moderately severe exercise, as in class work, the blood pressure taken immediately at the conclusion of the exercise shows, in the majority of cases, a rise, followed quickly by a fall to or near the normal or to subnormal, as indicated by my results, and those of others. In the exceptional cases when this does not occur, it may indicate that for these cases either the exercise, however mild it may seem, is too severe; or that it was taken in an exhausted condition; or, on the other hand, that those taking it were so well trained that the blood pressure was little if any influenced. Thus Pembrey and Todd⁷ found that with 2 men running up and down stairs, the one trained and the other untrained, the former showed a smaller rise and a more rapid recovery than in the case of the untrained man. Gordon⁸ narrates an interesting incident illustrating the effect of training in the case of the Champion Club Swinger of the World, Tom Burrows by name, aged thirty-eight years, a teacher of club swinging, swinging his clubs, weighing together three pounds, twelve hours continuously for six successive days. Readings of the blood pressure were taken daily before and after the twelve hours' swing, and on every occasion a rise of blood pressure was found at the close of his day's work, in one case the increase being 15 mm. Hg. This was apparently a case of light exercise long continued,

³ Edinburgh Med. Jour., 1907, xxii, 53.

⁴ Jour. Amer. Med. Assoc., 1909, liii, 195

⁵ Arch. Int. Med., 1910, p. 382.

⁶ Amer. Jour. Phys., 1911, xxvii, No. 5, p. 46.

⁷ Jour. Phys., 1908, xxxvii, 66.

⁸ Loc cit.

by a perfectly trained man, in whom the fatigue point was never reached, a little better than an equilibrium between fatigue and recovery. Cases 71 and 75 in my series, appear also to illustrate this effect of training.

These reasons, however, do not explain all the exceptional cases. Probably the size of the heart and its integrity, the condition of the nervous system, the lasticity of the arteries, the habits and artificial influences like alcohol and tobacco, the age, weight, and perhaps the mental state of the individual, are other reasons. In interpreting the variations of the blood pressure under physical exercise, all the conditions of the individual and his environment must be taken into account. These conditions are so complex and occult that we cannot yet wholly dissociate them or give each its true value.

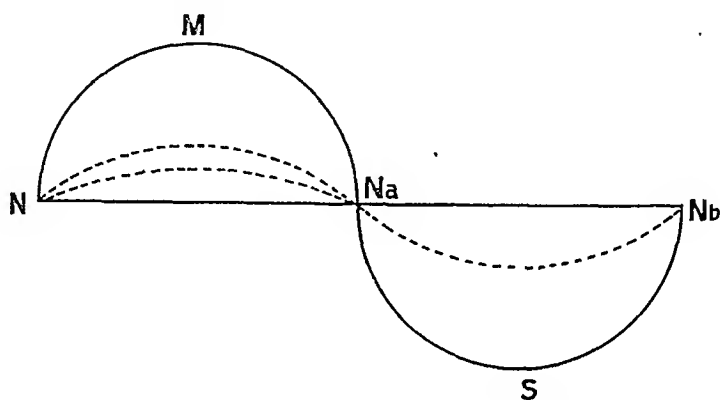
In my 126 cases of moderate general exercise, a mixture of various kinds, as in class work, 97, or 77 per cent. showed a rise of blood pressure immediately after the exercise. In 9, or 8.1 per cent., there was no difference between the first and second measurements; and in 20 cases, or 16 per cent. there was a fall in the second measurement. With the third test, taken from three to twenty minutes after the exercise, in some cases after a simple rest, and in others after the bath, out of 59 men, 45, or 76 per cent., showed either a fall to the initial measurement (supposedly the normal), or to a subnormal pressure, generally the latter. Of course, there is the possibility of error in the two latter measurements, the second and the third, in that the initial blood pressure might have been above the normal from some exercise previously taken, of which I was unaware, for it was difficult to always get the men perfectly fresh from a state of rest.

Reasons for these exceptional cases have already been suggested. To formulate, then, the results I have obtained, as well as those of other investigators, one may say that physical exercise in the majority of cases, of whatever nature it may be, excessive, severe, and long continued, or more gentle and moderate, causes a rise in the systolic blood pressure, the maximum occurring sometimes during the effort. As fatigue sets in and advances, the pressure falls to normal or subnormal. "A maximum systolic pressure," says Lowsley,⁹ is reached more rapidly in the case of a fatigued individual, but it is not nearly so extensive." If the exercise ceases at a time when the increased pressure exists, which is indicated by taking it immediately upon stopping exercise, the return toward the normal takes place rapidly, generally within a comparatively few minutes, as was the case with my observations. Or, if it ceases after the fall to subnormal has occurred, as in the case of more extensive fatiguing, and long-continued exertion, then the

⁹ *I. loc. cit.*

return *upward* to the normal is slower, depending upon the degree of fatigue and exhaustion. Lowsley considers the subnormal phase following the exercise as an important indication of the effect of the exercise upon the individual. "When," he says, "the subnormal phase returns to normal within sixty minutes, the exercise may be considered as lying well within hygienic limits for that individual; while a return that is delayed beyond 120 minutes may be regarded as exceeding these limits."

We may represent graphically the various phases of the blood pressure during and after physical exercise by a double curve.



Graphic representation of the various phases of the blood pressure during and after physical exercise.

Starting from the normal (*N*) for each individual, and rising until the maximum (*M*) is reached, at a greater or less height; remaining there for a greater or less time, according to the strength of the individual for sustained work, his condition of freshness or fatigue, and his degree of training; then, as fatigue begins and increases, falling and continuing to fall until the normal (*Na*) and subnormal (*S*) point is reached; and finally, after cessation of the exercise and rest, a return more or less rapidly, depending on the degree of fatigue, to normal again (*Nb*).

As will be seen, the majority of my cases, 77, or 76 per cent., represent what might be called the normal, using for the moment the word in another sense, and safe curve of exercise or physical exertion, namely, starting with the normal blood pressure; ending at or near the maximum; and then shortly, in a comparatively few minutes, returning to or near the normal again, it may be a little above or a little below. When this curve is obtained we may say that the exercise or effort is well within the strength of the individual. In certain cases, as I have already indicated, this curve may approximate to a straight line, or only the second curve, the fall from normal to subnormal and the rise to normal again, is found. The blood pressure taken at any period of time during the formation

of this double curve would appear to give some indication of the condition of the individual in relation to the exercise he is taking, and hence serve as a guide to the suitability of the exercise, both as regards severity and duration, or as regards his condition at the time of taking the exercise.

If, for example, immediately after exercise the blood pressure is subnormal and remains so for some time, as in the case of the Marathon runners and football players, or in any case, even if the exercise is moderate and not long continued, such as class work, then for that individual, or for his condition at the time of taking the exercise, we may consider the exertion too strenuous or too prolonged. To illustrate this I will refer to Case 100 of my series. This was a merchant, aged sixty-two years, of delicate build, who, after his day's work, took the class exercise. His initial blood pressure was 138, and immediately after his exercise it was 118, and he looked overworked and tired. It would appear to be a fair assumption that he was in a condition of fatigue at the commencement of his exercise, and hence what he needed was rest and not physical effort. Numbers 34 and 107 seem to be similar cases. In other cases the subnormal second measurement might be explained by the fact that the individual was untrained, and, therefore, more quickly reached the fatigue point. This may have been the case with the three police officers, Nos. 58, 59, and 86, who, after an hour's rather strenuous exercise at handball, showed a subnormal pressure. The case of the two boys, brothers, Nos. 92 and 93, is rather interesting. No. 92, though smaller and younger than 93, has always shown more endurance and vitality than his older brother; and I think the blood pressure measurements would give some indication of this fact, for at the close of the same class work the older showed only 3 mm. Hg rise in pressure, while in the younger it was 10 mm. Hg. Evidently one reached the fatigue point more quickly than the other. Furthermore, the last measurement after a bath showed a lower or at least a more lasting subnormal point in No. 93 than in No. 92.

The case of the 32 young women is interesting and suggestive. In the first place, it will be seen that all, from No. 16 to No. 32 inclusive, 17 cases, who made the short, severe exertion of running up and down stairs, or a rapid run around the track, showed, with one exception, a very much increased blood pressure immediately after their effort, which pressure fell, in from three to eight minutes, to subnormal in 11 cases, and at or a little above normal in the other 6. While, with the other 15 girls who took class work of one kind or another, 9 showed a slight rise of blood pressure immediately after the exercise, 4 a slight fall, and 2 no change. Ten minutes after the exercise, 11 showed a fall to subnormal, 2 were above normal, and 2 normal. It seems to me that a fair interpretation of the comparatively slight variations in the blood pressure of these last 15 girls is that they were well trained, taking

regular, systematic exercise daily, and, further, that they had frequent short rests during the class work. Doubtless other inferences will suggest themselves from this series of observations, but from what has already been shown, it seems to me to be a fair deduction that, taken in connection with other knowledge of the individual, his physical condition, habits, age, training, etc., the blood pressure, taken at the three periods mentioned, may be a valuable guide and aid in apportioning the proper amount of physical exercise to the individual, particularly when it can be so delicately applied as to foree, time, and variety as in gymnasium work under skilled supervision. Furthermore, by means of the indications given by the blood pressure, we may be enabled to avoid injury from excess, or from exercise unsuited to the individual.

Anything so sensitive to stimuli and perturbing influences, both within and without, as the blood pressure, must, of course, be subject to wide variations, and, therefore, we cannot expect it to be an accurate guide, but rather an aid of considerable value when taken in connection with other evidence. Panchon,¹⁰ who has published a series of observations upon the maximum and minimum blood pressure taken by an instrument of his own device, which he calls the "oscillometer," declares that the variations of the arterial pressure are valuable criteria in the application of physical exercise, and by them one can make a choice both of the kind and amount of exercise proper for each particular case. "The sphygmomanometric study," he continues, "constitutes a very sensitive criterion of the endurance of the organism during physical work." And with Gallic enthusiasm, he declares that such criteria ought to be applied wherever there is human activity, not only in the case of physical culture, but as well in industrial life, especially where the work should be exactly adapted to the endurance of the individual. Whether or not this French savant had ever heard of the present popular "scientific management" of industries, I do not know, but at any rate, his observations are suggestive in this direction, and it would appear reasonable and be an interesting study to apply his criteria, namely, the blood pressure measurements, to the workingman, if thereby we might more accurately determine his fatigue point, and apportion his work accordingly, and thus both conserve his energy and obtain his maximum efficiency.

I desire to express my obligations to Dr. Sargent, Director of the Sargent Normal School of Physical Education, in Cambridge, to Mr. Hibbard and his assistant, Mr. Browning, of the Young Men's Christian Union Gymnasium, and to Messrs. Roberts and Caswell, of the Young Men's Christian Association Gymnasium, both of Boston, for the very valuable aid they rendered me in making these observations.

¹⁰ Comptes-rendus de la Société de Biologie, May, 1910.

TABLE I.—Blood Pressure and Physical Exercise. Girls of the Sargent Normal School of Physical Education.

No.	Name.	Age.	Occupation.	Form of exercise.	Blood pressure before exercise.	Blood pressure immediately after exercise.	Blood pressure after a rest of from 3 to 20 minutes.	Remarks.
1	E. R.	20	Student	Class work with intervals of rest.	100	115	10 min. after exercise, 95	
2	E. C.	21	Student	Class work with intervals of rest.	114	117	100	The same girl after she had run up and down four flights of stairs had a blood pressure of 114, 140, 120.
3	N. H.	19	Student	Clubs and balls	100	115	100	
4	E. P.	21	Student	Class work	125	136	118	
5	C. P.	22	Student	Class work	120	5 min. after exercise, 117	113	After short, violent exercise the blood pressure was 150.
6	H. B.	23	Student	Class work	125	5 min. after, 115	112	After short, violent exercise, the blood pressure was 150.
7	L. T.	19	Student	Class work	100	115	88	
8	L. G.	22	Student	Class work	90	115	114	
9	H. B.	23	Student	Dancing	114	100	100	The second blood pressure was taken after violent dancing and the third two minutes later. The second blood pressure was taken after violent dancing.
10	E. G.	27	Student	Dancing	90	100	88	
11	D. R.	21	Student	Dancing	115	114	117	
12	I. T.	22	Student	Dancing	94	94	94	
13	L. C.	21	Student	Bounding balls	90	95	85	
14	E. B.	19	Student	Dancing and chestw'ghts.	115	115	90	After violent class dancing the second blood pressure was 150.
15	G. L.	21	Student	Clubs and balls	120	122	115	Another blood pressure was taken after brisk exercise and measured 120.
16	M. B.	19	Student	Running up 4 flights of stairs and back	102	130	100	
17	D. Y.	22	Student	Running up 4 flights of stairs and back	115	140	After 5 min. rest, 100	
18	E. A.	27	Student	Running up 4 flights of stairs and back	112	134	115	
19	M. P.	21	Student	Running up 4 flights of stairs and back, twice	90	130	90	
20	F. C.	20	Student	Running 2 laps	114	130	100	
21	K.	21	Student	Running 3 laps	138	158	130	
22	M.	21	Student	Running 4 or 5 laps	120	160	100	
23	C.	21	Student	Running 2 laps	108	122	90	
24	D.	20	Student	Running 2 laps	130	170	130	
25	H.	20	Student	Running 2 laps	118	130	115	
26	W.	20	Student	Running 2 laps	115	118	110	
27	N.	22	Student	Running 3 laps	110	160	115	

TABLE I—(Continued).

No.	Name.	Age.	Occupation.	Form of exercise.	Blood pressure before exercise.	Blood pressure immediately after exercise.	Blood pressure after rest from 3 to 20 minutes.	Remarks.
28	C.	20	Student	Running laps	3 112	152	118	
29	E.	21	Student	Running laps	4 117	158	112	
30	S.	19	Student	Running laps	3 115	140	118	
31	F.	20	Student	Running laps	3 120	152	115	
32	B.	19	Student	Running laps	3 117	140	116	
	G.	27	Pianist	Played piano for one hour for class	124	120	120	

TABLE II.—Blood Pressure and Physical Exercise. Gymnasium Members. Men.

No.	Name.	Age.	Occupation.	Form of exercise.	Blood pressure before exercise.	Blood pressure immediately after exercise.	Blood pressure after rest of from 3 to 20 minutes.	Remarks.
33	B.	30	Gymnasium instructor	Class work	128	140	135	Taken at another time, it was 120, 120, 135.
34	T.	21	Waiter	Class work	123	120	120	This man works all night and then comes to the gymnasium.
35	R.	31	Dentist	Class work	120	130	116	
36	W.	39	Business	Class work	115	160	117	
37	D.	49	Real estate	Class work	130	140	132	
38	B.	39	Metal polisher	Class work	142	142	115	He had probably been doing some work before the first measurement was taken.
39	McA.	45	Journalist	Class work	139	130	125	He had probably been doing some work before the first measurement was taken. Taken again, the first measurement was 130.
40	J.	37	Baggage master	Class work	115	120	115	
41	P.	53	Shoemaker	Class work	130	160	130	
42	McC.	21	Student	Class work	114	118	110	
43	R.	62	Dentist	Class work and running	140	180	140	
44	W.	28	P. O. clerk	Run a mile	130	185	130	
45	S.	57	Locomotive engineer	Class 15 minutes	140	140	140	Taken another time 145, 145, 120.
46	R.	27	Physical director	Dancing	130	150	120	
47	C.	28	Clerk	Class	140	160	130	Worked all the previous night.
48	F.	22	Waiter	Class	130	150	117	
49	W. A. S.	36	Police inspector	Hand ball	120	130	115	Smokes immoderately.
50	C.	26	Gymnasium instructor	Class and dancing	125	138	118	
51	L.	31	Chauffeur	Class work	138	158	125	
52	S.	19	Stamper	Class work	115	150	112	

TABLE II—(Continued).

No.	Name.	Age.	Occupation.	Form of exercise.	Blood pressure before exercise.	Blood pressure immediately after exercise.	Blood pressure after rest of from 3 to 20 minutes.	Remarks.
53	C.	30	P. O. clerk	Class work and a hard $\frac{1}{4}$ mile run	130	180	114	The third measurement was taken one-quarter of an hour after bath.
54	D.	18	Clerk	Class work	138	180	130	
55	R.	36	Gymnasium instructor	Running 4 laps	120	140	114	
56	V.	19	Gymnasium helper	Running 3 laps	110	154	120	
57	S.	37	Salesman	150	140	138	The last measurement seven minutes after exercise.
58	M.	30	Police officer	Half hour hand ball	115	100	90	
59	G.	33	Police officer	Half hour hand ball	128	120	120	
60	R.	33	Jeweler	100	115	100	
61	R.	26	Salesman	148	168	134	
62	K.	27	Clerk	110	118	116	
63	H.	40	Gymnasium instructor	Dancing and heavy dumb-bells	125	140	120	Taken again, 118, 140, 122.
64	B.	29	Student	Class work	120	132	118	Had been doing some work before first measurement.
65	K.	21	At service	Class work	100	115	116	
66	B.	35	Salesman	Class work	117	155	125	
67	C.	41	Masseur	Giving massage briskly	145	170	150	
68	L.	49	Business Clerk	Class work	130	170	120	Probably had been doing some work before first measurement.
69	C.	26	Clerk	Class work	145	140	140	
70	M.	29	Electrical engineer	Class work	100	115	100	Well trained. Exercises three, four or more times a week. Night work.
71	E.	30	Lawyer	Class work	130	130	120	
72	S.	33	Stationary engineer	Chest w'ghts. and dumb-bells	120	120	117	First measurement after some exercise.
73	L.	21	Waiter	140	138	138	
74	B.	20	Attendant	130	115	115	
75	S.	20	Stenographer	Class work	130	140	130	
76	S.	29	Journalist	Class work	120	134	130	No exercise, but massage.
77	L.	24	Clerk	Was given brisk massage	115	115	117	
78	S.	25	Clerk	Class work	120	140	120	Had taken some exercise before first measurement.
79	S.	30	Bookkeeper	Class work	130	150	120	
80	M.	25	Electrical engineer	Brisk, severe, short exercise	115	140	117	
81	R.	26	Clerk	Class work	120	150	120	
82	G.	17	Apprentice	Class work	130	130	115	Had taken a walk before the first measurement. Uses alcohol and tobacco to excess.
83	L.	25	Draughtsman	Chest w'ghts. and mat work	117	130	115	
84	L.	28	Police officer	Hand ball	115	118	100	
85	McG.	36	Police officer	Hand ball	140	150	125 to 138	
86	D.	36	Police officer	Hand ball	135	130	120	
87	P.	39	Ry. P. O. clerk	Hand ball and dancing	100	115	115	
88	C.	19	Student	115	112	115	
89	C.	40	Lawyer	130	150	132	
90	R.	59	Clerical	Rowing	130	140	125	

TABLE II—(Continued). Boys.

No.	Name.	Age.	Occupation.	Form of exercise.	Blood pressure before exercise.	Blood pressure immediately after exercise.	Blood pressure after a rest of from 3 to 20 minutes.	Remarks.
91	D.	15	Apprentice	Class work	100	108	100	Had been wrestling before the first measurement.
92	E. O.	11	School	Class work	114	124	110	
93	J. O.	13	School	Class work	112	115	95	
94	M.	14	School	Class work	125	118	95	
95	H.	11	School	Class work	98	110	98	
96	S.	13	School	Class work	117	110	100	

TABLE III.—Blood Pressure and Physical Exercise. Gymnasium Members. Men.

No.	Name.	Age.	Occupation.	Form of exercise.	Blood pressure before exercise.	Blood pressure immediately after exercise.	Remarks.
97	S.	20	Clerk	Class work	112	126	This man looked overworked and tired out.
98	K.	36	Salesman	Class work	110	118	
99	C.	28	Clerk	Class work	122	150	
100	T.	62	Merchant	Class work	138	118	
101	D.	49	120	140	Exercise had been taken before both of these blood pressures.
102	J.	39	Musician	145	150	
103	S.	19	Class work	100	115	
104	D.	34	Attorney	Class work	120	130	
105	L.	31	Banker	Pull ups and dips	160	180	
106	M.	38	Salesman	Class work	120	128	Says he is overworked in mind and body.
107	M.	30	Attorney	Class work	125	115	
108	P.	37	Weigher	Class work	116	116	
109	S.	37	Salesman	Class work	132	140	Weight 190. Not used to much exercise.
110	W.	39	Hotel keeper	115	112	
111	R.	49	Merchant	140	148	120.
112	S.	46	Physical director	130	142	
113	R.	50	Merchant	130	160	
114	H.	39	Police officer	120	150	
115	S.	43	Merchant	130	160	120.
116	L.	22	Class work	108	140	
117	W.	23	Chest w'ghts.	120	115	
118	B.	20	Class work and running	122	160	
119	B.	18	Class work	138	158	Played ball before first blood pressure.
120	C.	28	Class work, slight	112	120	
121	D.	18	Class work, slight	140	142	
122	M.	24	Class work, slight	150	184	
123	P.	22	Class work	140	170	
124	F.	30	Class work	94	120	
125	A.	19	Class work and running	140	190	
126	H.	61	Running 2 to 3 laps	158	192	

REVIEWS

A MANUAL OF PRACTICAL HYGIENE FOR STUDENTS, PHYSICIANS, AND HEALTH OFFICERS. By CHARLES HARRINGTON, M.D., late Professor of Hygiene in the Medical School of Harvard University. Fourth edition, revised and enlarged by MARK W. RICHARDSON, M.D., Secretary to the State Board of Health of Massachusetts. Pp. 850; 124 illustrations and 12 full-page plates. Philadelphia and New York: Lea & Febiger, 1911.

WITH the increasing interest in preventive medicine there has been an increasing demand for works on hygiene, which is in reality the science of prevention of disease. Many of these works have been either too elementary and general or too technical and limited in their field of application to be of any great service to the clinician or the general practitioner. The present volume wisely takes a middle course. It deals with the subject of hygiene and its closely related branches in a thoroughly scientific and detailed manner, but yet in terms easily within the grasp of the average clinician and covers the host of subjects in the one volume for which several reference books would usually be necessary.

The advances in the subject have been so rapid and the applications of hygiene to the prevention, etiology, and cure of disease have been so increased and widened in recent years that rather frequent revisions of such works are necessary. The present work, representing the fourth edition of this book, was begun by Dr. Harrington before his death and completed by Dr. Richardson. The authors have aimed to bring the work thoroughly up to date and to make it as far as possible "an authoritative guide for all classes of readers interested in hygiene and sanitation."

The book may be divided into two parts. The first of 409 pages discusses in its four chapters the fundamental subjects of Foods, Air, Soil, and Water. Each chapter is full of information of a very practical nature, not only for those dealing directly with hygienic problems, but also for the general practitioner who cannot handle and treat diseases intelligently without applying the principles here given. The first chapter on foods contains considerably more than a discussion of their purely hygienic bearing, and gives much information as to the use of food in the preservation of health and in the treatment of disease. In the other three chapters the dis-

cussion covers many of the border line subjects not directly touched on by works on medicine, chemistry, physics, or bacteriology.

The second part of the book, 381 pages, takes up more specifically the application of hygiene in its many various phases. Here are discussed habitations and sanitation, disposal of garbage and sewage, disinfectants and disinfection, military, naval, marine, and tropical hygiene, the relation of insects to human disease, personal and occupational hygiene, vital statistics, immunity, and vaccination, quarantine, and disposal of the dead. In each of these chapters will be found in considerable detail, and yet in a comparatively concise form, the main information usually sought for under the respective headings. In many instances brief *resumes* are given of the laws governing these various hygienic subjects. Concrete examples are quoted from literature to point out the dangers of unhygienic methods or the advantage of proper procedures. The work is unusually complete when the breadth of the subject is considered; it is well written, very readable, and contains few typographical errors. The directions and conclusions are based on sound principles and study, and may be relied upon.

Some of the subjects discussed may, at first glance, seem hardly related to hygiene, and yet the author in every case makes clear the definite bearing of these subjects to the cure or prevention of disease.

The book has well fulfilled its mission and should prove interesting and helpful to any one interested in the subject of hygiene or the still broader one of medicine.

F. H. K.

DIET IN HEALTH AND DISEASE. By JULIUS FRIEDENWALD, M.D., and JOHN RUHRÄH, M.D. Third edition; pp. 765. Philadelphia and London: W. B. Saunders Company, 1909.

THROUGH some complication the review of this admirable book is late in appearing. This edition, the third, is entered abreast of the times and differs from its predecessor in as much as the articles on milk and on alcohol have been rewritten and additions to the articles on tuberculosis, salt-free diet, rectal feeding, and caloric needs of infants have been made. Many other important tables have been inserted, for instance, that showing the caloric value of foods and that of Winton on the composition of diabetic foods. One criticism might be made of these tables, and that is, that calories are reckoned on the "fuel value per pound" method, instead of the far easier, far preferable, and more widely used method of fuel value per gram.

This edition maintains the same high standard of the first and second editions, and its features are terseness and cleanness of description with a wealth of detailed diets. The authors have succeeded in offering a work invaluable to the practising physician to whom it is heartily recommended.

E. H. G.

SURGICAL AFTER-TREATMENT. A MANUAL OF THE CONDUCT OF SURGICAL CONVALESCENCE. By L. R. G. CRANDALL, A.M., M.D., Assistant in Surgery at Harvard Medical School. Pp. 803; 265 illustrations. Philadelphia: W. B. Saunders Company, 1911.

THIS excellent work admirably serves the purpose for which it was written—to place in the hands of house surgeons in hospitals and of general practitioners in communities which are not surgical centres, a series of suggestions, based on experience and on common sense, as to the after-care of surgical patients. This is, however, the author's too modest estimate of his own achievement. It might well be added that there are few operating or consulting surgeons who would not be benefited by occasional reference to this book.

It is certainly true that as years and experience increase, the busy surgical practitioner tends—like every worker in any department of human endeavor—to become more rigid and less flexible, to be guided more and more by habit and routine, and finally, as self-confidence justifiably develops, to become unwittingly more or less impervious to new ideas. He may, and usually must, be familiar with the latest improvements or the differing methods in operative and aseptic technique, but he is too apt to lose sight of the details—often all-important—of the patient during the after-period, when the prompt recognition and skilful treatment of conditions easily manageable in their incipency prevent them from becoming threatening or fatal.

Perfunctory advice to the general practitioner, the interne, or the nurse who has the continuous charge of the case, is worse than none, as in the absence of individual experience they often follow blindly, with a sort of military discipline, directions that have become inapplicable or even harmful. Reference to such a book as this, on the part of all concerned, would in many cases avoid these dangers, would give the relatively inexperienced a safe guide in many critical conditions, and would often suggest to the operator or consultant alternatives that might otherwise be forgotten or might be outside his own personal experience.

The scope of the book is catholic and the subjects dealt with

vary from thirst, pain, sleep, hiccough, diet, bedsores, rectal feeding, bandaging, massage, and such obvious generalities, to specific operations on all the important organs and regions of the body.

The first part contains, in addition to the above articles, chapters on various relatively recent surgical methods, such as the Bier hyperemic treatment, saline fomentations, x-ray and radium therapy, etc.

The second part is equally up to date and shows on every page familiarity with the practice and the records of the most recent operative procedures. Throughout the book there is an absence of dogmatism, an effort to deal judicially with opposing views, and a display of common sense in the advice offered that is noteworthy and is much to be commended.

The hackneyed remark that "no surgeon's library should be without this book" might well be expanded to include the libraries of all who have anything to do with the after-treatment of surgical cases.

J. W. W.

A TEXT-BOOK OF MEAT HYGIENE. WITH SPECIAL CONSIDERATION OF ANTEMORTEM AND POSTMORTEM INSPECTION OF FOOD-PRODUCING ANIMALS. By RICHARD EDELMANN, Ph.D., Medical Counsellor; Royal State Veterinarian of Saxony; Professor at the Royal Veterinary High School in Dresden. Authorized translation, revised for America, by JOHN R. MOHLER, A.M., V.M.D., Chief Pathological Division, U. S. Bureau of Animal Industry, and ADOLPH EICHHORN, D.V.S., Senior Bacteriologist, Pathological Division, U. S. Bureau of Animal Industry. Pp. 392; 152 illustrations and 5 colored plates. Philadelphia and New York: Lea & Febiger, 1911.

THAT a second edition of Mohler and Eichhorn's translation of Edelmann's Meat Hygiene has been called for is very encouraging, since it may be regarded not only as an evidence of approval of the work, but also as an indication that this division of public hygiene is receiving at least a portion of the attention it deserves.

The general arrangement of the material is the same as in the first edition, but a few parts which have become obsolete have been omitted, while new facts, established since the earlier publication, have been added. Portions of the book have been rewritten, and where this has been done there has been a gain in clearness and conciseness, although the first edition was by no means deficient in this respect.

Involving as it does certain facts connected with the physiology of the meat-producing animals and the parasitology, bacteriology, and pathology of the diseases affecting them, the decomposition

processes to which meat and meat products are liable and the methods of preservation, together with the sanitation of abattoirs, etc., the subject of meat hygiene is not one that lends itself readily to discussion in a single volume, but in this book all of the principles underlying the rational practice of meat hygiene are presented concisely, and yet comprehensively, in less than 400 pages, adapting it for use as a work of reference as well as a text-book. These basic principles are, of course, as applicable in the United States as in Germany, but the text of the original German work has been supplemented by such additions as are necessary because of the differences in the practice in this country and in Germany.

The regulations governing the meat-inspection service of the United States Department of Agriculture and a chapter on the organization and the methods of procedure of the Federal inspectors have also been inserted. This material, together with the chapters on the origin and source of meat food, the production, preparation, and conservation of meat, and the construction of abattoirs and stockyards, should be of especial interest to health officers or others in charge of the enforcement of local meat-inspection laws, and also to those who may contemplate the organization of local inspection systems; while practising physicians will find information of value in the chapters on the postmortem changes of meat and on meat poisonings. The other portions of the book are of especial interest to veterinarians engaged in the practice of meat hygiene.

The book is printed in clear type on good paper and is substantially bound, while the text is illumined with instructive illustrations. The requirement of a second edition in this country is but a repetition of the history of the book in Germany, where the first edition was soon exhausted.

L. A. K.

THE PRINCIPLES OF PATHOLOGY. By J. G. ADAMI, M.A., M.D., LL.D., F.R.S., Professor of Pathology in McGill University, and ALBERT G. NICHOLLS, M.A., M.D., D.Sc., F.R.S. (Can.), Assistant Professor of Pathology and Lecturer in Medicine in McGill University, Montreal. Second edition. Vol. I, pp. 1027; 329 engravings and 18 plates. Vol. II, pp. 1160; 301 engravings and 15 plates. Philadelphia and New York: Lea & Febiger, 1911.

A LITTLE more than a year ago the writer published in this JOURNAL a brief note appreciative of Dr. Adami's volume on general pathology, and of the volume on systemic pathology prepared by the same author in collaboration with Dr. Nicholls. Continued use, often daily, in the interim has rather added to his realization of the monumental character of the work; and the additions and occasional

recastings of isolated sections in the second edition, which has been before the profession for the last year, confirm the general impression which the first appearance of the volumes made. It stands to-day as not only the most compendious statement of our knowledge of pathology which has originated from the press of this continent, but also as the most satisfactory and logical discussion of the intricate problems of disease and the most suggestive work upon the general subject which has been presented by any of the pathologists writing in the English tongue. This assertion applies particularly to the first volume, that upon general pathology, in which the principles of the subject are discussed. The application of anything like the same mode of presentation to the multitudinous subdivisions of the systemic part, even were the writers to successfully avoid the indefinite repetitions so liable to occur, would have increased the work to prohibitive size; and the authors seem entirely justified in leaving such application to the reader in large measure.

The general plan of this edition remains unchanged from that of the first. Technical methods have no part in the work; for these the student must consult works on technology. And, particularly in the volume on general pathology, anatomical details appear only as a part of the presentation, satisfactory but succinct; and the real effort of the work lies clearly along the dynamic line, in the setting forth of the problems concerned in the developments of these visible changes, the factors involved, the modes of their influence, and the effects of the established changes. In the volume on systematic pathology this is naturally to a large extent reversed, and the work follows more closely the many excellent existing works descriptive of organic changes, each section, however, having an important introduction devoted to the more prominent physiological problems involved.

The first volume, after a brief chapter of definition and general orientation of the subject matter, takes up at length, as a necessary preparation, the subjects of cell structure and relation, and of the chemical and physical activities of the cell, this leading through cell multiplication into sexual reproduction and inheritance. In this first section of the volume, comprised in fifteen chapters, the author condenses with rare ability our knowledge of living matter, as fundamental to what is essentially a work upon the diseased living body rather than a mere statement of the morphology of the dead remnants of disease. In this section the most important new matter is that dealing with the part played by the nucleus in cellular functions. Briefly stated, the author would grant to the nucleus not only its well known part in maintenance of cellular life and multiplication, but also an important role in cellular metabolism, acquiring material for its own growth and activity from the cell body, and at the same time transmitting substance

to the latter essential to the functional activity of the cytoplasm, whether secretory, neural, motor, excretory or otherwise. The material in the appendix of the first edition upon the classification of the proteins is transferred to an appropriate chapter in the introductory division of this volume. Fuller consideration of the chemistry of the lipoids; material additions to the subjects of fertilization, the contribution of the cytoplasm of the germ cells to the developing offspring, and other matters of inheritance, are notable in this second edition.

The changes in Section II, dealing with the causes of disease, include fuller discussions of such factors as temperature, light and the special light rays, electricity, and nutritional faults. In the third section additional matter and more or less revision are met in the parts dealing with immunity, complement fixation, and the Wassermann reaction; in the recognition of a class of neurinomas, to include the cutaneous neurofibromas; and in the group of the hyaline degenerations, from which the author separates another of the hyaloids under the name elastoid degeneration, referring to the hyaloid masses met not infrequently in vessel walls, as of the arteries of the myometrium of women who have borne children.

In the second volume the major changes appear in the various introductory paragraphs to the different systems and organs, as fuller presentation of the physiological disorders and their results. They constitute in the aggregate, but a minor part of the volume, but are invariably illuminating and valuable. It seems to the reviewer that along this line increasing value for future editions may be accomplished, if necessary, with some sacrifice to descriptive sections. Unquestionably it is this feature which is most urgently required in our texts upon systemic pathology, bridging the gap which is still too apparent between the excellent and numerous works upon morphological pathology and the works upon the application of medical science.

Increase in text-references and in illustration adds materially to the excellence of the volumes; and, although there is evidence of some haste in the preparation of the books in the rather numerous typographical errors, their general appearance is to be commended, the publishers having well supported the authors in their efforts in making a creditable presentation of this magnificent work.

A. J. S.

HYDROTHERAPY. By GUY HINSDALE, M.D. Pp. 466; 145 illustrations. Philadelphia and London: W. B. Saunders Company, 1910.

To those who are familiar with the patient study which the science of hydrotherapy has received from investigators in Germany,

Austria, and in France, it must remain, and probably will forever remain, a riddle why we, of this enlightened Western continent, have persistently refused to recognize the subject. The word "recognize" is advisedly used, and we understand by this term an appreciation of the importance of hydrotherapy with the subsequent application of this knowledge as a remedial measure. We pride ourselves as a nation, on our bodily cleanliness, and the home without the shower or the tub is to us a home unblessed with the Lares and Penates of good health. Why is it that with the recognition given water as a means of preserving health we have failed to support its claims as a curative measure, and have, wittingly or not wittingly, refused to advocate its employment in combating disease?

There can be but one answer to this pertinent query, and that is ignorance on the part of the American physician as to the advantage to be derived from hydrotherapy. It has been employed notably in the treatment of typhoid fever, and in the management of certain kinds of cardiac inefficiencies, but with the exception of these two instances and a few minor inconsequential examples the practice is far from universal.

In the work under review Hinsdale has achieved a creditable ambition, namely, to guide the growing practice of hydrotherapy and balneology along rational lines. He has contributed his not insignificant share to this end, and this work reflects great credit on its writer. The book is divided essentially into four parts, although they are not so figured by the author: General hydrotherapy, under which the rationale of the method and its physiology are discussed; special hydrotherapy, which is devoted to a consideration of every disease at all likely to be benefited by the use of waters; technique of hydrotherapy, where are given the multitudinous techniques of applying water; and finally, the internal use of mineral water, a section describing, in a few pages, the internal use of waters in various diseases. In addition to these main headings, there are a few pages devoted to prescriptions for hydrotherapy, and a reprint of an address delivered by Dr. Baruch on "Some Truths about Hydrotherapy."

One of the most pleasant impressions derived from a careful perusal of this book is that hydrotherapy, for its usefulness, does not depend on magnificent marble-lined baths equipped with marble-topped tables surmounted by an armamentarium of brilliantly polished nickel spigots, and supplied with various highly attuned mechanical devices for registering temperature and pressure of the water. These have been the development of the science, but the field of usefulness may still be harvested in a homely fashion by the use of homely inventions with beneficent results.

The author has drawn freely on literature for aid in the preparation of the book, and the illustrations have been gathered from

many sources, making the work broad in scope and adequately rich in pictorial reproductions. Not "to those especially interested" is the valuable volume referred, but to all physicians who seek knowledge regarding this greatest of physiological therapeutic measures, Dr. Hinsdale's book is highly recommended.

E. H. G.

THE SURGERY OF THE DISEASES OF THE VERMIFORM APPENDIX AND THEIR COMPLICATIONS. By WILLIAM HENRY BATTLE, F.R.C.S., Surgeon and Joint Lecturer on Surgery to St. Thomas' Hospital; and EDRED M. CORNER, M.A., M.B., M.C., F.R.C.S., Surgeon in Charge of Out-patients and the Surgical Isolation Wards, to St. Thomas' Hospital. Second and Enlarged Edition. Pp. 291; 100 illustrations. New York: William Wood & Co., 1911.

THE second English edition of this well-known monograph appeared a year ago, the preface being dated April, 1910; and the American edition follows about a year later, as was the case with the first edition (1904, 1905). The volume is larger by nearly one hundred pages, and shows evidence of thorough revision, amounting in many places to complete re-writing.

The authors appear even more certain, than when writing their first edition, of the predominant frequency of chronic lesions, believing that these are the main predisposing factor for acute attacks. An entirely new section has been introduced, discussing the increase in appendicitis in recent years (an increase which they believe is not merely apparent), and suggesting as a cause the almost universal use in civilized communities of wheat ground in rolling mills; the theory is proposed that in such wheat there are contained extremely minute particles of iron or steel, broken off the fluted rollers, and that these, entering the digestive tract, may lodge in the appendix, may there produce an abrasion, and so may create a *locus minoris resistentiæ*, whence infection arises. They say: "A statement was recently made on the authority of an American physician in an English paper that appendicitis was caused by white flour. The reasons given were the following. When white milled flour was introduced into the cities of a certain State appendicitis began to be prevalent, but it was not yet found in the country. As it became cheaper it was introduced into the villages, and appendicitis became common there, yet the negroes escaped. When, however, the flour became so cheap that it was more profitable to buy it than to grind the corn at home, then negroes began to suffer from appendicitis. It must not be forgotten," continue the authors, "that the greater prevalence of appendicitis was heard of first in the United States, from which so much of our flour comes,

before we saw much of it, and it had been a good deal written about over there before the reason for doing so was apparent by any increase of the disease in this country. A few years ago windmills were conspicuous in every landscape in England, and our corn was ground between stones in the districts where it was grown. It can no longer be ground by the old methods at a profit, and flour mills are only to be found in the towns, worked by machinery. Now much of our supply comes ready for the market from beyond the seas, and it is mostly ground up by metal rollers." As a confirmation of this theory the authors quote one case, a patient subjected to operation in 1905, in the centre of a concretion from whose appendix a small piece of iron was found.

Battle and Corner urge operation in all acute cases within the first forty-eight hours, because they believe the total mortality is thus very much reduced; and while they acknowledge that many patients will survive an acute attack without removal of the appendix, they contend that "if operation should be called for after the third day, it cannot but be felt that the case would have been far better treated had it been so submitted earlier." They do not recommend the removal of the appendix in bad abscess cases at the first operation, if it is difficult to find it; but if the appendix is not removed when an abscess is opened, it should be removed as soon as possible after healing of the abscess. They urge earliest possible operation in cases with unlocalized peritonitis; removal of the appendix is the first step; a large incision is advised, with eventration of the intestines and puncture and evacuation of the distended coils. "The advocate of evisceration," they say, "is held up rather as a kind of vivisector who does a dreadful thing. Now, there can be no question that operation in these cases should be performed quickly, and if there is plenty of assistance and warm saline fluid, the parts may be cleansed much more efficiently and in far less time when the bowels are prolapsed than by pulling up the intestine and wiping it in sections; and we maintain," they continue, "that the shock is often less than that produced by the more prolonged operation. Too much time must not be expended in trying to wipe off lymph," etc. *Too much time*, indeed. Why waste any time at all? Why not adopt the American operation for the American disease? Why not get in and get out as quickly as possible, removing the cause of the disease and instituting drainage through a small incision, without evisceration, and without perfectly useless and utterly destructive efforts at cleansing the intestines? We are unavoidably reminded of the caustic saying of the wisest of men: "The beginning of the words of his mouth is foolishness, and the end of his talk is mischievous madness."

Yet useful suggestions in the treatment of peritonitis are the "axillary infusion" of Corner, and the use of a rigid tube for proctoclysis. In the former method a puncture is made with a scalpel in

the skin over the pectoralis major muscle; a trocar and cannula are then thrust through the fibers of this muscle into the cellular tissue of the axilla; this method is advised as easier of execution than intravenous infusion, and as allowing the introduction of larger quantities of saline solution than hypodermoclysis; it is stated that by this method one of the authors has seen two pints of saline solution given and largely absorbed in ten minutes. In giving saline solution by the rectum they recommend the use of a pewter tube one foot in length and half an inch in diameter, having a slightly bulbous extremity, with numerous openings; this is passed into the rectum "for about two to three inches, and is bent sharply at the anus so as to lie easily on the bed." They believe that a rigid tube such as this allows more saline to be administered, as kinking is impossible; and they claim to have no difficulty in introducing by this means at least a pint of fluid every hour.

The use of stock vaccines and sera they characterize as a "shot in the dark," while before autogenous vaccines can be prepared the patient may be dead. Of nucleic acid injections, they say "it may help him to recover, but it will not compel him to recover."

Under differential diagnosis no mention is made of septic renal infarct, though numerous other kidney lesions are discussed; and in the section on the differential diagnosis of peritonitis and intestinal obstruction the value of auscultation in detecting peristalsis is not mentioned.

If this work had been written in Australia or South Africa, the reviewer might be tempted to characterize it as provincial; what to call it when emanating from the centre of civilization, he knows not.

A. P. C. A.

A TEXT-BOOK OF GENERAL BACTERIOLOGY. By EDWIN O. JORDAN, Ph.D., Professor of Bacteriology in the University of Chicago, and in the Rush Medical College. Second edition; pp. 594; 162 illustrations. Philadelphia: W. B. Saunders Company, 1910.

AN index to the satisfactory character of Jordan's Bacteriology is found in the fact that since its first publication in 1908 it has been twice reprinted and now comes forth in second edition. While incorporating the chief of the newer advances in this field, the author has wisely refrained from greatly altering the plan or increasing the size of the book.

The pathogenic microorganisms receive the greatest amount of attention, and the descriptions are, in general, lucid and sufficiently detailed for the purposes of a text-book, though not infrequently lacking in specific points sought by the worker in this field. As

such may be mentioned a more nearly adequate discussion of the pleomorphism of the colon-typhoid group, and a recognition of the close resemblance between the pneumococcus and the streptococcus with the differentiating characters. Chapters on technique and the general principles underlying the subject form the introductory part of the book, and toward the end there is a brief consideration of the pathogenic protozoa, moulds, and fungi, and of the bacteria of water, air, milk, and plant diseases. On the whole, such omissions as may be noted are usually the result of studied scope, and in its field, which is to present in clear, readable, and comprehensive form the essentials of the more important aspects of bacteriology, the book is to be warmly commended. For the student it is unexcelled.

D. B. P.

THE MEDICAL RECORD VISITING LIST OR PHYSICIANS' DIARY FOR 1912. Revised edition. New York: William Wood & Co., 1912.

PHYSICIANS have always had the reputation of being poor business managers. This is due partly to the nature of their work and partly to unsystematic methods. Any means, therefore, which will serve to simplify and yet keep accurate the business side of medical work should be gladly welcomed. Many of the methods suggested to-day for the keeping of records of daily visits are too cumbersome and detailed and if tried are soon given up and abandoned. The present edition of the Physician's List for 1912, has met the problem of record keeping in a perfectly simple, accurate, and systematic way. The book is so arranged that rather detailed records of the visits of 60 patients per week may be kept without confusion, and a note made of future visits. In a short printed section in the first part of the book are tables of weights and measures, an extended list of remedies and their maximum doses which is very complete and accurate, methods for treating various emergencies, artificial respiration, and several minor subjects. The book is neatly bound in red leather and is of a serviceable size and shape.

F. H. K.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

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Secondary Infection in Pulmonary Tuberculosis.—ROSWELL T. PETTIT (*Jour. Infect. Dis.*, 1911, ix). The degree of importance of secondary infections in pulmonary tuberculosis is disputed. Some consider the tubercle bacillus as responsible for practically all the pathological conditions of a tuberculous lung; others believe that secondary invaders, more often streptococcus, pneumococcus, or staphylococcus play a large role. Between these two extremes are those who assign a certain importance to both. Previously in attacking the problem, seven methods of attack have been employed—clinical observation, animal experimentation, bacteriological and anatomical examination of lung post mortem, or of sputum ante mortem, study of opsonic indices and of leukocytes, and finally of blood cultures. In reviewing the literature, varying results are reported by different observers. In regard to blood cultures, the findings of which have been long recognized as constituting most direct evidence, the varying results may be explained by technical differences. The earlier observers drew blood from the ear or finger, with a large percentage of positive results; while later workers have used venous blood with a small positive percentage. Pettit has studied 130 blood cultures, using a large quantity of blood (5 to 20 c.c.) from a vein, planting it on the most favorable media, and incubating for at least forty-eight hours. As possible contaminations, he has excluded all growths of any organism but pneumococcus or streptococcus, which he has differentiated by cultural and microscopic appearances, and reaction on serum-inulin agar or in serum-inulin water. As control, he has studied the blood of 21 normal individuals, using the same technique, all with negative results. He has obtained positive cultures in 46 per cent. of 130 cases, growing streptococcus from 36 patients, and pneumococcus from 24. Considering the results from other points

of view, Pettit has found that of incipient cases, 16 per cent. were positive; of advanced, 45 per cent.; and of far advanced, 68 per cent.; of patients with an afternoon temperature below 100°, 34 per cent. showed positive blood cultures, as compared with 58 per cent. in those with higher afternoon temperatures. He concludes that the isolation of pneumococcus or streptococcus from the blood in so many cases shows that not only are true secondary invaders of frequent occurrence in pulmonary tuberculosis, but that often such organisms constitute a complication of great pathological significance.

The Incoagulable Nitrogen of Puncture Fluids, with Special Reference to Cancer.—From recent observations, that malignant tumors contain one or more proteolytic enzymes, ROGER S. MORRIS (*Arch. Int. Med.*, 1911, viii, 457) considered that primary or metastatic growths affecting serous surfaces might secrete their ferment directly into the serous cavity and fluid occupying it. That in those fluids resulting from pressure on vessels there should then be an absence of this ferment. In certain cases, therefore, there might well be an increase in the incoagulable nitrogen. With this idea in view, Morris has examined 25 fluids, removing the coagulable proteins according to the method of Hohlweg and Meyer, slightly modified. This consists, in brief, of precipitating the proteids by a reagent of acetic acid and monocalcium phosphate, and sodium chloride, and testing the filtrate for nitrogen by Kjeldahl's method. From the literature and his own cases, Morris has selected 78 observations. The fluids are divided into three groups according to their content in incoagulable protein, the nitrogen being expressed in grams per cent. Group I contains incoagulable nitrogen of 0.0699 gram per cent. or less; Group II, 0.07 to 0.0899 gram per cent.; and Group III, 0.09 to 0.1 gram or more per cent. Morris concludes that in analyzing these groups with reference to cancer, Group I contains 4 of cancer out of 59 fluids; Group II, 2 cases of cancer out of 5; and Group III, 3 of cancer out of 4. It thus appears that a puncture fluid with incoagulable nitrogen below 0.07 gram per cent. is probably not of malignant origin; while a very high percentage of incoagulable nitrogen is, to say the least, a suspicious circumstance.

Nephritic Edema.—P. SCHMID and SCHLAYER (*Deutsch. Arch. f. klin. Med.*, 1911, civ, 44) have made an experimental study of nephritic edema in rabbits. It had previously been shown that two types of experimental nephritis could be differentiated, not on anatomical but rather on functional grounds. The one presents a severe lesion of the tubules with secondary affection of the circulatory apparatus—"tubular" nephritis. The second variety, the "vascular," is characterized by a rapid and intense injury to the renal vessels. In these two types of experimental nephritis the present observations were made. Their purpose was not to study the role of the kidneys themselves, but rather to determine the part played by prerenal factors, namely, the functional activity of the bloodvessels of the body and that of the tissues. The method of approach was as follows: Hyper- and hypotonic solutions of sodium chloride were injected subcutaneously. The hemoglobin and blood chlorides were determined before, immediately after the

infusion, and again at the end of one-half an hour. To eliminate diuresis as a factor, and to throw the full burden on the circulation and tissues, only those nephritic animals were used which had become completely anuric. Preliminary observations were made on (1) normal animals, (2) on those whose ureters had been ligated, and (3) on nephrectomized rabbits. To produce tubular nephritis, they employed potassium chromate; vascular nephritides were caused by arsenic, cantharidin, and uranium. The results which Schmid and Schlayer report cannot be given in the detailed form which their importance would seem to warrant. Briefly stated, they are as follows: The distribution of salt and water between blood and tissues differs when the kidneys are mechanically removed from the conditions found in experimental nephritis. In purely mechanical removal of the kidneys, the adjustment following injections of salt solutions is abnormally delayed; the blood retains unusually large quantities of water and salt. In the nephritides, the distribution of the injected solution varies according to the kind of nephritis under consideration. In the tubular nephritides (potassium chromate) one sees the same accumulation of water and salt in the blood that occurs in nephrectomized animals, but at the end of the experiment practically all of the solution has passed from the blood into the tissues. Here, then, there is an alteration in the sense of a slightly increased permeability of the vessels, following the primary collection of both water and salt in the blood. In the vascular nephritides (produced by arsenic, cantharidin, and uranium) the conditions are quite different. With increasing intoxication there is observed a correspondingly marked inability on the part of the vessels to retain water and salt in the blood; there is a total inability on the part of the vessels to remove the fluid from the tissues; finally, the permeability of the vessels for water and salt becomes so great that the infusion of salt solutions of high concentration no longer produces any change in the composition of the blood. These facts support the view, Schmid and Schlayer believe, that nephritic edema is caused through the coördination of a vascular lesion with an alteration of the body tissues. It is impossible to say whether the vascular condition is primary or whether both vessels and tissues are equally affected by the nephritic toxin.

On the Bence-Jones' Body.—R. MASSINI (*Deutsch. Arch. f. klin. Med.*, 1911, civ, 29) reports investigations made on a patient whose urine contained Bence-Jones' protein. Three lines of study were followed, and it was found (1) that a certain parallelism exists between the quantity of protein taken with the food and that of the Bence-Jones' body in the urine. This, therefore, points rather to a transformation of the food proteins into Bence-Jones' protein than to a production of the latter from marrow or tumor cells. (2) By means of deviation of complement with highly potent sera, it was possible to show definite quantitative differences between blood serum and Bence-Jones' protein. (3) Studies of the solubility of pure Bence-Jones' protein showed that the concentration of salts and acid determine largely its precipitability. Slight changes in concentration suffice to produce marked alterations in its coagulability. In this way Massini explains the contradictory reports in the literature on the more or less complete solution of the precipitate on boiling the urine.

SURGERY

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The X-rays in Renal Tuberculosis.—VON LICHTENBERG and DIETLEN (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiii, 739) in 11 cases of renal tuberculosis, showed the urinary path by the x-rays and the injection of a collargol solution. In the 8 unilateral cases nephrectomy was performed and the x-ray findings controlled by those of the extirpated kidneys. Of the 3 bilateral cases, in one a nephrotomy was performed. The radiographing of the renal pelvis or pyelography is beset with certain difficulties, although for the most part they can be overcome. The method stands or falls with the passage of the ureteral sound, which is often difficult or may be impossible. There is further difficulty in evacuating the kidney. The pelvis and calyces are filled with pus and caseous debris, as well as the tuberculous cavities which open into the calyces by a very narrow communication. In such cases the ureteral catheter must be left in longer (up to an hour) before the taking of the x-ray. Repeated aspiration aids, and a concentrated collargol solution should be employed, as it will mix itself with the caseous material and permit a fair shadow. If the collargol solution is introduced before the pelvis is evacuated, the shadow will not be clear. The collargol was usually employed in a 10 per cent. solution. The results of its use show that in many cases the diagnosis of renal tuberculosis is corroborated, and in many it is established, by this method. The radiograph produced is a typical one for this disease, and gives a fairly exact outline of the anatomical area affected.

Concerning the Pathogenesis of Acute Pancreatic Diseases.—PÓLYA (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, xxiv, 1) undertook to determine by experiments on dogs whether the albumin digesting pancreatic ferment, trypsin, can produce pancreatic diseases; and whether substances having a digestive action on albumins can do likewise. He found that trypsin solutions, having a powerful digestive action on albumins, as well as active pancreatic secretion, when injected into the pancreas, produce severe changes in the gland, such as hemorrhage, necrosis and its consequences, fat necrosis, and death. Inactive fistula secretion and weak or inactive trypsin solutions do no damage to the pancreas. Even strong trypsin solutions lose their pathogenic effects from being heated. The disease-producing agent is the proteo-

lytic trypsin. From the injection of intestinal contents, especially contents of the duodenum, into the pancreas, there were produced in a large number of dogs acute pancreatic necrosis and hemorrhages with fat necrosis; while in another group there developed cases of chronic interstitial pancreatitis. The effects of the intestinal contents and extracts of the mucous membrane were due chiefly to the bacteria cultures and bile mixed with them, which stimulated the pancreatic secretions. Upon the trypsin depended the disturbance of the gland and its deleterious effects. The valves at the opening of the pancreatic duct into the duodenum could hardly admit enough duodenal contents to produce the necessary stimulation of the pancreatic secretions. The damaging effect is, therefore, produced most surely by the trypsin solutions; less by the duodenal contents and bacteria-bile mixture; rarely by the contents of intestinal fistulæ; and only exceptionally by bacteria alone. The gap between the pancreatic ferment theory and the microparasitic theory is bridged by the recognized influence of the bacteria. Both theories, as well as the results of the pathologico-anatomical, clinical, and experimental investigations, will be brought into accord by the conception that the pancreatic destruction in acute pancreatitis is due to autodigestion of the gland, this being due chiefly to the action of the bacteria.

Immediate and Remote Results of Fifty-seven Nephrectomies for Renal Tuberculosis.—BOECKEL (*Ann. d. mal. d. org. gén.-urin.*, 1911, ii, 175) reports an interesting and detailed study of 57 nephrectomies performed by Andre, which were followed carefully for varying periods up to nine years. There were 31 males and 26 females; the youngest was aged thirteen years, the oldest, fifty-four years; the right side was involved 28 and the left 29 times. The kidney was primarily involved, at least clinically, in a large number, and when the genital apparatus was attacked, it was for the most part secondarily to the kidney. The nephrectomy was performed by the lumbar route 56 times, and only once by the transperitoneal route, in which case the operation was primarily done for a probable ovarian cyst, but an ectopic tuberculous kidney was found. In 5 cases the nephrectomy was secondary, one ten years after an operation for renal calculus, and in the 4 others after nephrotomy for pyonephrosis, the interval between the nephrotomy and nephrectomy being from a month to seven weeks. In 15 cases the nephrectomy was a subcapsular one, because of intense perinephritis, the perinephric fat being extirpated as freely as possible. A general uterectomy was not done, the ureter merely being drawn into the wound and divided as low as possible with a thermocautery. The immediate operative results were 55 cures and 2 deaths, one being independent of the operation and the other due to a general tuberculous infection six weeks after the operation. After a transient oliguria, following the operation, the quantity of urine rapidly returns to the normal in most cases, and in a few there is polyuria. Free drainage was always employed. The wounds were closed in from fifteen days to twenty months after operation. The best results in hastening the closure of tardy fistulæ were obtained with Beck's bismuth-vaseline paste. There were 9 secondary deaths. One patient died two and one-half years after the nephrectomy, which had been followed by much

amelioration of the disturbances, the patient dying of pulmonary and intestinal tuberculosis. Another died at the end of five years from uremia. The autopsy showed an atrophic nephritis of the remaining kidney, which as well as the bladder were tuberculous. The 7 others died within a year after operation, the disease having existed in all a long time before, making them unfavorable cases. Only one of these was autopsied, and showed a pulmonary tuberculosis. Of the remaining 46 cases, 5 were only transiently ameliorated. The other 41 were much improved or were completely cured. All have been examined recently or have been heard from. In 7 the operation had been done from five months to a year; in 15 from one to two years; in 12 from two to four years; and in 7 from four to nine years. They are all in a much improved general condition, and all have gained weight, one as much as 30 kilograms. Many have returned to their work, sustain fatigue, and one has, without inconvenience, gone through a period of military service. In 31 of the 41 pain in the bladder has disappeared completely, in 8 it is much ameliorated, and in only 2 is it only slightly ameliorated. In nearly all there is an increased capacity of the bladder. In many cases it was found that the tuberculous lesions had completely disappeared, in some shown by a cicatricial condition of the ureteral meatus, and in others by the completely normal condition of the bladder. In 24 of the 41 cases the urine became completely clear, in 9 it was turbid, and in 8 not completely transparent. In 12 of the 41 pus was found in the urine by the microscope, and in 26 no pathological elements. Briefly, the results show 2 operative and 9 later deaths, 4 mild ameliorations, and 41 positive ameliorations and cures.

Bacteriological Examination of the Blood in Anthrax.—BECKER (*Deut. Zeits. f. Chir.*, 1911, cxii, 265) says that in every fatal case of anthrax the bacilli of anthrax can be found in the blood in life. In every body dead of anthrax they can be found in large numbers. Their presence in the blood gives a bad prognosis. Of 11 cases in which the bacilli were found in the blood, 9 died. One was saved by giving salvarsan intravenously. To determine the value of a method of treatment (*e. g.*, by serums) a bacteriological blood control is necessary, since severe cases with negative blood findings heal spontaneously. The results of the bacteriological examinations of the blood speak for conservative as against operative treatment for malignant pustule.

Experimental and Literary Studies Concerning Extensive Resections of Small Intestine.—SOYESIMA (*Deut. Zeits. f. Chir.*, 1911, cxii, 425) says that there are many opinions as to how much intestine may safely be removed in man. He did resections of the intestine on 11 dogs in an effort to solve the problem. In an extensive resection, the severity of the operation is best determined by the relative length of the resected portion than by the absolute length, since the total length of the jejunum-ileum is very variable. Brenner's case, in which 83.6 per cent. of the small intestine was removed, is the most extensive successful resection on record. Under favorable circumstances one can resect in dogs up to 90 per cent. of the total length of the jejunum-ileum without great disadvantage. From clinical experience and

experimental results, Soyesima believes that the resection of up to 80 per cent. in man, is a permissible operation. A compensatory hypertrophy or dilatation of the remaining intestine usually occurs in those animals which withstand the operation well, while it does not occur in those which do not long outlive the operation. Distinctions as to prognosis, according to the segments of the intestine removed, were not demonstrable.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Quartan Malaria with Salvarsan.—REICH (*Therap. Monatshefte*, 1911, xxv, 594) reports a case clinically diagnosed as quartan malarial fever that yielded promptly to an injection of 0.6 gram of salvarsan. This patient had reacted only slightly to treatment with quinine. The symptoms have not recurred in a period of four months' observation after the injection.

Soy Bean Cookery.—RUHRÄH (*Med. Record*, 1911, lxxx, 626) gives a number of recipes for the preparation of the soy bean that are especially adapted for diabetic patients. The soy bean is an annual leguminous plant that is extensively used in China and Japan, where it has been a staple article of food for centuries. It has great nutritive value, being especially rich in fat and protein content. The fact that the soy bean has only a small percentage of cane sugar in its composition makes it most valuable in the dietary of diabetics. The beans may be cooked in soups, baked, or boiled with salted meats, etc. It is a good plan to first soak the beans for eight or ten hours, after which the firm outer skin will separate and can be removed easily. A flour has also been manufactured from the bean that may be prepared in a great variety of ways. Ruhräh gives recipes for utilizing this soy bean flour in gruels, soups, muffins, nut cakes, pan cakes, etc.

The Practical Application of a Salt-poor Diet.—LEVA (*Med. Klin.*, 1911, vii, 1582) gives a long list of various seasonings that may be used to replace the lack of salt in a salt-poor dietary. Among these are mint, thyme, capers, onions, celery, cress, lemon, vinegar, mustard, caper sauce, tomato sauce, and mayonnaise. He also says that the free use of sugar and cream enables patients to dispense with salt to a considerable extent. Leva has experimented with the substitution of sodium bromide for salt in the seasoning of bread, eggs, soups, and vegetables. It does not taste like salt, but the patients can apparently dispense with salt more easily when it is given than without its use.

He does not believe that any harmful action will result from giving amounts of from 1 to 2 grams of sodium bromide a day. His experiments proved that sodium bromide increases the elimination of sodium chloride, and thus indirectly of dropsical fluid. Therefore the addition of sodium bromide to the diet serves to aid the dietetic treatment of dropsical conditions.

Clinical Results of the Treatment of Gout and Other Joint Affections with Radium Emanations.—GUDZENT (*Berlin. klin. Woch.*, 1911, xlviii, 2098) has treated a number of cases of gout and chronic arthritis, due to various causes, with radium, and believes that this method of treatment is based upon true rational therapeutics. The most notable result of the treatment of gout by radium, in addition to the clinical improvement, was the effect observed in diminishing the amount of uric acid in the blood. In a majority of the cases the uric acid completely disappeared from the blood in a comparatively small number of treatments. Gudzent believes that the radium treatment promotes the solubility and destruction of urate deposits in the body, and he also assumes that the radium has a stimulating action upon the function of the tissue enzymes. Gudzent says that radium is best given by inhalation, and he gives details of the proper dosage and method of administration. He thinks that a purin-free or purin-poor diet is often a valuable aid in the treatment of gout, but it is impossible to rid the blood of uric acid by dietetic measures alone. Therefore, he would not subject patients to the hardships of a purin-free diet, but would exercise certain limitations in the diet as determined by the individual case. It is not important to continue a purin-poor diet if no effect is observed from its continued use over weeks or months. He advises the addition of colchicum or atophan to the treatment during acute attacks of gout. Mild and moderately severe cases of chronic progressive polyarthritis, especially the variety occurring in children, were very favorably influenced by this treatment. The emanations have little or no effect when the joint process has reached the stage of marked deformity or ankylosis. No effect of the treatment was observed in joint affections due to syphilis or tuberculosis, but gonorrheal arthritis was often considerably improved. Gudzent says that it is often a good plan to combine the treatment by radium emanations with local injections of soluble radium salts in the neighborhood of the affected joints. The employment of local dressings wet in radio-active solutions will often relieve pain and tend to hasten the cure.

The Influence of Treatment on the Wassermann Reaction in Syphilis.—MATSON and REASONER (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1670) believe that the Wassermann reaction not only reveals the nature of the disease, but it serves as a guide for individualizing treatment. It has shown the necessity of more energetic and individual treatment than has been the custom heretofore. Fully half of the patients discharged as cured are only half way to their goal, and in reality are latent syphilitics. The early administration of mercury may cause a disappearance of manifestations, with little influence on the spirochetes, the organisms remaining latent for years, and under

favorable conditions renewing their activity with reappearance of manifestations. A positive reaction may be made to disappear by energetic, specific treatment, and this sustains the conclusion that a positive reaction means active syphilis, even though there be no other evidence, and speaks for renewal of treatment. Patients who have been well treated give negative reactions, whereas those poorly treated give positive reactions even years later. The number of inunctions or injections of mercury or salvarsan injections necessary to convert a positive into a negative reaction varies with each patient, and should be controlled by the blood examination. A positive reaction in tabes is little affected by treatment. If mercury is used, systematic and consecutive treatment is necessary, and this should be begun early, and during the first year no lapses of over one month permitted, or much that has been gained will be lost. The use of alcohol has a bad effect on syphilis, predisposing to secondary and late manifestations, and, to a certain extent, nullifying the treatment. In patients recently treated by mercury, and giving a positive reaction, the time required for a negative Wassermann with salvarsan may be much reduced. In very recent cases, or older cases not under the influence of mercury, there may be no shortening of the time. In cases of a mercury-produced Wassermann negative at the time of injection, the reaction will generally revert to a plus-minus, or in some cases to plus, and then at varying intervals go back to negative, from which subsequent injections may not change it. This is suggested as a possible diagnostic procedure in cases in which the question of a cure is open to doubt and it is not desired to suspend treatment if the infection still persists. The intravenous method of giving salvarsan is to be preferred to others as being easier, more efficacious, less painful and requiring less time on the part of the patient. At least two injections should be given, and more if indicated, and these injections should be given about a month apart. An otherwise healthy adult will take from 0.5 to 0.6 gram intravenously without bad effect. Unless one is prepared to maintain a very thorough watch over the patient, the salvarsan treatment should be reinforced with mercurial medication, and in any event better results will be obtained thereby. Matson and Reasoner believe that a positive Wassermann is a sign of active syphilis, irrespective of clinical manifestations. They have observed that there has been a return of the reaction from negative to a partial-positive or positive reaction in 22 per cent. of cases under observation for seven months. This may be explained by insufficient treatment or by the fact that a persistent negative reaction could not be obtained in alcoholics even when the treatment was energetic. A certain number of syphilitics have a constant positive Wassermann reaction in spite of the most active treatment. This fact points to an unfavorable prognosis, and it is thought that many of these patients subsequently develop paresis and ataxia.

The Treatment of Pleurisy.—ARNSPERGER (*Therapie d. Gegenwart*, 1911, lii, 495) reports in detail 7 uncomplicated cases of pleurisy with effusion, and 4 complicated cases treated by early aspiration of the effusion followed by the injection of from 150 to 600 c.c. of nitrogen into the pleural cavity. He believes that both pleural adhesions

and a return of the pleural exudate are prevented by this method. The amount of nitrogen introduced into the pleural cavity must not be large enough to cause any compression of lung substance, and consequently it is better to control the amount injected by a fluoroscopic examination at the time of injection. The procedure had to be repeated two and three times in 3 of Arnspurger's cases, but no untoward effects were observed from these injections. Arnspurger also combined this method with autoserotherapy, injecting subcutaneously from 1 to 3 c.c. of the patient's own exudate as the needle was withdrawn from the pleural cavity.

PEDIATRICS

UNDER THE CHARGE OF

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Secretion of the Mammary Glands in Infants an Index to the **Mother's Nursing Power**.—K. BASCH (*Münch. med. Woch.*, 1911, lviii, 2266) calls attention to the fact that there occurs in infants a secretion of milk from the mammary gland similar to that occurring in the nursing mother. This activity of the mammary gland occurs in both male and female infants, and the secretion morphologically shows the same elements as mothers' milk—free fat droplets and white blood cells. The most plausible explanation for this secretion in the newborn child is advanced by Knöpflemacher, who holds it is due to a physiological process, and that the same stimulus which starts the mother's milk secretion also starts that of the child. He was unable, however, to verify this by animal experimentation. By injecting extracts of embryos, endometrium, and ovaries from pregnant animals into virgin animals, a proliferation of the mammary gland substance was demonstrated, but never a secretion of milk. The author, however, has been able to accomplish this by injecting placental extract into non-pregnant animals, which had, however, been pregnant at some previous time. The same result, in lesser degree, was obtained in animals which had never been pregnant before. In all these cases of milk secretion, however, there was no accompanying mammary hyperplasia, such as occurs physiologically during lactation. This hyperplasia was finally accomplished by implanting an ovary from a pregnant animal into a non-pregnant animal. The hyperplasia, plainly apparent and proved by microscopic tests, followed the course usual to a pregnant animal of that species; but when the maximum was reached secretion of milk was not forthcoming. If then placental extract was injected, the milk secretion appeared. Therefore Basch concludes that the mammary hyperplasia in pregnancy is set up by stimulating substances arising in the ovary, while the incidence of the milk secretion is caused by similar substances arising from the matured placenta. Basch applied

this explanation to the problem of milk secretion in infants. By using placental secretion on infants in which a preceding mammary secretion had normally disappeared, he was able to stimulate the milk secretion again. While Henoch and other authorities state that the mammary secretion begins usually on the fourth day and ends about the twentieth day after birth, Basch has frequently seen the secretion in infants three, four and one-half, and five months old. By comparing the degree of mammary reaction in a large number of infants to the quality and the supply of the mother's milk, Basch has found that there exists a parallel between the two. So that, in general, an early and free mammary secretion in the infant prophesies an accompanying rich and sufficient maternal milk secretion. This fact was apparent in a series of 100 cases especially studied. A weak or absent reaction in the infant, however, does not imply, with as much certitude, a weak or failing maternal supply.

The Standard Role of the Salts in Mother's Milk in Infancy and Childhood.—HANS FRIEDENTHAL (*Münch. med. Woch.*, 1911, lviii, 2385) remarks on the growing disinclination of women to nurse their infants, with the result that in Germany, at least, only a small and constantly diminishing percentage of infants get the benefit of mother's milk during the first nine months of life. In the necessary substitution of nourishment for mother's milk the most important factor—that of the proper combination of the salts—has been very little emphasized. Cow's milk, fortunately, comes nearest to human milk in its salt content. The standard of absolute ash-content in milk is the rapidity of skeletal growth. Human milk contains the least percentage of ash, since the growth of the human skeleton is the slowest of all skeletal animals. Therefore, within physiological limits, a milk rich in ash will stimulate skeletal growth and vice versa. The salts of calcium especially, and of iron are important factors in this connection. Different specimens of human milk differ in 50 per cent of cases in their ash content, but show considerably less difference in the proportion of their salts. Cow's milk, to have the same proportion of calcium as human milk, must be diluted more than five times. But with this dilution the proportions of sodium and potassium are reduced 4 per cent. and 31 per cent. respectively, below those of human milk. So that in practice it is impossible in any way to get the same proportion of salts in cow's milk by dilution. Only by the addition of the deficient elements can the difference be equalized. If there is a deficiency of one important inorganic element such as potassium, for instance, no other salt in any proportion can make up for or take the place of the deficient element. The loss of 3 mg. of iron from a liter of infant's nourishment continually would mean a slow but inevitably fatal result. The proper proportion of inorganic elements in an infant's nourishment is, therefore, of the first importance. Friedenthal believes it is of the greatest importance, practically to exhibit the salt content of human milk in the child's nourishment, not only during the first months of life, but during the entire physiological suckling stage of three years. A system for its practicable application is highly desirable.

OBSTETRICS

UNDER THE CHARGE OF

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Double Congenital Dislocation of the Hip and Its Effect upon the Pelvis.—DELMAS (*L'Obstétrique*, August, 1911) gives the results of his studies of 17 pelvises with double congenital dislocation at the hip-joints. In these cases the pelvis is tipped very strongly forward, but is not uniformly narrowed except above the brim of the true pelvis. The actual pelvic brim is somewhat enlarged transversely, as is the case with the pelvic cavity below the brim. Occasionally in these cases the whole pelvis suffers from general atrophy. The pubic arch is usually wider than normal. The sacrum is pushed upward and back, and the pressure of the thigh bones separates the ilia, making the crests straight and the intercrest diameters about 22 cm., and the distance between the spines 22.5 cm. The outlet of the pelvis is larger than normal, especially transversely, and this is true the older the patient, possibly due to the thinning of the pelvic bones. The pelvic cavity is made larger, and those diameters which are most increased at the brim are the transverse and oblique. The same thinning process is seen in the wings of the ilia, and many of the bony lines of the pelvis are poorly marked. The abnormalities found in the pelvis in these cases seemed to result from the absence of the force normally transmitted through the necks of the femora.

Pituitrin as a Stimulant in Labor.—STERN (*Zentralbl. f. Gynäk.*, No. 31, 1911) gave pituitrin in doses of 0.6 gram in prolonged labor as a stimulant to uterine contraction. In these cases he is in the habit of giving a prophylactic dose of some preparation of ergot after delivery, to avoid possible relaxation and postpartum hemorrhage. Labor may also be induced in some cases by giving pituitrin. In a patient with tuberculosis of the larynx and lungs, 0.6 gram was given at the thirty-sixth week of pregnancy, followed by gradual development of the first stage of labor. The injection was repeated with further progress, and two others were finally given, followed by normal expulsive contractions and the birth of living twin children, mother and children making a good recovery. In another patient suffering from nephritis there were threatening symptoms of eclampsia at the thirty-ninth week. During four days, six injections of pituitrin, 0.6 gram, and one of 0.1 gram, were given, followed by spontaneous normal labor. In another case of severe tuberculosis pregnancy was terminated at the end of eight months, and two doses of 6 cm. failed to produce pains. Then 1 c.c. was given seven times, followed by weak and deficient contractions for a few hours. An injection of 3 c.c. produced no better effect. A bag was then inserted for six and one-half hours without result. One cubic centimeter of pituitrin was then given, and the pains became

vigorous, and after eleven hours the bag was expelled, followed by the child in breech presentation. In these cases the uterine contractions were not of the tonic variety. There was always an interval between the pains, so that no injury to the fetus resulted. It seems especially valuable in cases of nephritis with threatened eclampsia. In two cases of pregnancy in the early months pituitrin failed to produce abortion. In one patient with incomplete abortion it caused uterine contraction.

Pregnancy Complicated by Acromegaly.—MAREK (*Zentralbl. f. Gynäk.*, No. 47, 1911) reports the case of a primipara aged twenty-six years. In childhood she had measles and scarlet fever. Menstruation began at twelve, and was normal. The first half of pregnancy passed without disturbance. At about the eighth month the patient felt as if her clothing had become much too tight. The fingers became so thick that her rings could not be worn. Pain developed in both lower extremities; the patient was weak, drowsy, and very thirsty. The quantity of urine was gradually increased. The face was greatly altered, the nose and lips increasing very evidently in size. There was no headache or disturbance of vision. The patient developed also coryza and hoarseness. On examination there was no exophthalmos, but the nose was greatly enlarged, broad, and very hard. The lips were thickened and projected outward. The tongue was thickened. the lower jaw projected beyond the upper, the teeth closing badly. The thyroid could be palpated as somewhat enlarged; both tonsils were enlarged and reddened; the thoracic viscera seemed normal. The pulse was 120, strong, and full. The hands were greatly enlarged, apparently by thickening of the tissues, the skin seeming to be infiltrated and very hard. So far as could be made out, there was no alteration in the bones of the fingers. A similar condition existed in the toes, while the skin of both lower extremities was thickened. Edema, however, was absent. The fundus of the uterus was three fingers' breadth above the umbilicus, the fetus in second position, and the head presenting. The urine contained no albumin, but gave a very positive reaction to sugar. The patient went on for some time, feeling fairly well, without any especial alteration in her condition. The membranes ruptured and very slight pain developed, which after some days became vigorous. The head failed to descend, the heart sounds became irregular, the caput increased, and the patient was delivered by forceps. The placenta was readily delivered. The child cried lustily. After delivery the patient's temperature rose somewhat, the pulse was 128 and strong. During the first few days of the puerperal period the patient was depressed, and especially complained of great thirst; up to the eleventh day the urine gave a positive reaction for sugar. The pulse gradually became less frequent, and on the eighteenth day the patient got up. She complained of pain in both lower extremities and in both hands. The symptoms of acromegaly gradually disappeared during the puerperal period—the thickening of the skin in the lower extremities—and the intense thirst passed away within the first three days after confinement. The face slowly assumed its normal condition, and the nose and lips ceased to be enlarged. There remained, however, deformity of the lower jaw, and the teeth did not close properly. The abnormalities in the fingers and toes remained the longest, and the

patient could not wear her rings for some months after her confinement. The sugar gradually disappeared from the urine without any modification in the patient's diet. The patient nursed her child, and the child did well. Marek considers this a case of increased action and secretion of the hypophysis, with increased adrenal secretion also. He remarks that cases of pregnancy having sugar in the urine may be divided into three groups: In one the sugar is milk sugar, which is very constantly found. In a second group the sugar is not milk sugar, but its presence in moderate quantity is not accompanied by a disturbance in the patient's health. Before conception occurred these patients had no sugar in the urine, and it disappeared soon after confinement. In a third group of cases, the patients have sugar in the urine before conception occurs, and it persists throughout the gravid state. The reviewer has recently had under his observation an interesting case of toxemia, accompanied by the prolonged presence of sugar in the urine. At the latter portion of the sixth month a multipara became drowsy, weak, and complained of excessive thirst. The urine showed a considerable percentage of sugar, with casts and albumin. There was some nausea and headache. There were also slight uterine contractions which threatened the interruption of pregnancy. These symptoms gradually subsided in severity under careful diet and constant and skilled nursing. In spite of a vigorous hygiene the urine did not become normal. The patient delivered herself at two hundred and ninety days of a living child, weighing 8.5 pounds, who shared in some degree the symptoms of the mother. The child's hands and feet were swollen soon after birth, its urinary secretion was deficient and highly colored, and its intestine contained much dark and disintegrated matter. Both mother and child improved steadily after birth.

The Mortality of Parturition.—UNTERBERGER (*Archiv f. Geburts. u. Gynäk.*, 1911, Band xcv, Heft 1) has endeavored to classify those conditions which most frequently cause mortality in parturient women. These statistics are gathered from a portion of the German Empire. He finds that 1 death in 488 births occurs from puerperal septic infection; 1 in 1480 births from tuberculosis; 1 in 1948 from eclampsia; 1 in 3454 from embolism; 1 in 3759 from postpartum hemorrhage; 1 in 4291 from placenta prævia; 1 in 8170 from nephritis in pregnancy; and 1 in 10,892 from atony and shock.

The Pelvic Kidney.—In the *American Journal of Obstetrics*, October, 1911, Bissell, of New York, contributes a second paper upon this interesting subject. From 1910, he reported the case of a patient whose pregnancy was complicated by dislocation of the kidney into the pelvis; and he adds other cases in his experience, aggregating 3 in all. These conditions may require Cesarean section at the time of labor, and can be successfully dealt with by a plastic operation, which in one or more steps replaces the kidney to nearly its normal position. The obstetrician must not lose sight of the fact that a pelvic tumor complicating labor, and obstructing delivery, may be a dislocated kidney, and that such a tumor should not be removed until no doubt exists concerning its nature. If it be the kidney, delivery should be effected by Cesarean section and the kidney replaced.

GYNECOLOGY

UNDER THE CHARGE OF

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Endometritis.—An attempt to gather together and unify the modern consensus of opinion on this much discussed subject is given in a recent article by ALBRECHT (*Monatsschr. f. Geb. u. Gyn.*, 1911, xxiv., 397). The general principles of Hitchmann and Adler's work have been confirmed, he says, though the cyclic endometrial changes cannot be quite as sharply classified as those authors wish. The endometrium is subject to periodic changes due to the internal secretory activity of the ovaries, but the individual type of these periodic changes varies greatly. In principle it consists in an increase in the vital function of the corpus glands, evidenced by an increase in the volume of the epithelium, hypertrophy of the glands, and increased secretion, especially in their basal portion. The stroma takes part in the process by undergoing a decidua-like change. The development of these menstrual glands occurs irregularly in the uterus, and they do not all collapse and empty their secretion during menstruation, as Hitchmann and Adler claim, but some of them can persist throughout. This irregularity is due to the fact that the periodic functional activity of the ovaries, and also the responsiveness of the endometrium, are variable. It is, therefore, impossible to judge of the exact phase in the individual case from the appearance of the endometrium. Since "endometritis" means merely an inflammation of the uterine mucosa, and since the chief changes take place here in the stroma, the term "interstitial endometritis" is tautological, and should be given up. Etiologically endometritis may be divided into (1) bacterial, (2) toxic (due to chemical substances, necrotic tissue, toxins of infectious diseases, etc.), (3) mechanical and thermal. Since, however, all these causes produce identical conditions in the endometrium, a different classification is necessary for practical purposes. The most satisfactory from this point of view is that into (1) acute, (2) chronic, and (3) specific. In acute endometritis the alterative and exudative changes predominate over the proliferative. There is cloudy swelling, desquamation, even necrosis of the epithelium, swelling and increased secretion of the glands, as in all inflammations. Active hyperemia is present, with escape from the vessels of serum and leukocytes. The increased quantity of leukocytic infiltration in the tissue is the chief criterion of inflammation. Other infiltration cells (lymphocytes, plasma cells, etc.) are in the background as compared to the leukocytes in acute endometritis. This condition may heal or become chronic; that it so often does the latter is due to the unfavorable conditions for healing presented by the recurring increase in congestion and functional activity of the endometrium at each menstrual period. In chronic endometritis we have much less exudation of serum, or none at all; the cellular infiltrate

consists chiefly of round cells, with some plasma and mast cells, but few leukocytes. The plasma cells, while usually present, are not characteristic for chronic inflammation, however, as they may be absent, and, on the other hand, they can occur without inflammation. Here the proliferative changes are the important ones. There is an increase of connective tissue in the stroma, especially around the bloodvessels. Atrophic and hypertrophic areas may alternate. The bloodvessels show tortuosity, thickening of the walls, proliferation of the endothelium. The surface epithelium may take on a many-layered character, and become squamous in type. The glands show proliferation, with increased activity, and may extend deep down into the myometrium. Under specific endometritis are classed tuberculosis and the few definitely demonstrated cases of syphilitic endometritis. The diagnosis "endometritis" is only to be made when all the complex of tissue changes associated with inflammation are present; all the hyperplastic conditions without inflammation, formerly described as "endometritis glandularis hyperplastica," are to be considered as pure hypertrophies. They have nothing to do with inflammation, but the symptoms of both may be practically identical.

Electricity in Gynecology.—PETTIT (*Rev. pratique d'obst., de gyn., et de p  d.*, 1911, No. 7, p. 193) emphasizes the value of electricity in conservative gynecological therapeutics. Its chief action is hemostatic; indeed, the rapidly interrupted, tetanizing faradic current is such a rapid and sure hemostatic that it is suitable for use in emergencies to stop a sudden hemorrhage. For the permanent cure of hemorrhage, however, the constant current should be used, this being applied to the interior of the uterus. It has a caustic action, causing coagulation of the blood and destruction of the mucous membrane, resembling the action of the thermocautery. It has also a decided excitomotor action on the muscle fibers of the uterus, which, of course, increases its hemostatic effect. When an intra-uterine electrode of copper, zinc, or silver is used, and is made the positive pole, as it should be in treating hemorrhage, it can be demonstrated that ions of these metals are driven off into the mucosa, and exert there their coagulating and hemostatic effect as well. This form of treatment is applicable to many forms of hemorrhage, but it is especially valuable in the metrorrhagias of young women, in whom curetting leads to but temporary improvement. The action of electricity on fibroids seems to be rather irregular and uncertain; for these *x*-ray treatment seems to offer better results. The electric current, in addition to its hemostatic and excitomotor properties, has analgesic, bactericidal, and disinfectant actions, and is, therefore, of great use in treating leucorrh  as. In cases of amenorr  as due to infantile uterus, Pettit says that electrical treatment often works wonders, causing an increase in the size of the uterus, and sooner or later the appearance of menstruation. Atresia of the cervix may also be overcome by intracervical electrolysis, utilizing for this purpose the well-known dilating properties of the negative pole; frequently a metal electrode will penetrate when all other attempts at dilatation have been in vain.

Tuberculosis of the Female Genital Organs.—MEYER (*Gyn. Rundschau*, 1911, v, 716) reports his experience in 40 cases of tuberculosis of the lower abdomen operated upon in the Tübingen Gynecological Clinic during the last four years. These fall almost equally into two chief types: (1) Outspoken and predominant adnexal disease, the adnexa often being the size of fists, with no involvement of the peritoneum other than intestinal adhesions. (2) Outspoken peritoneal disease, with ascites or tubercles on the peritoneum, the adnexal involvement here being often very slight, with merely small swellings or tubercles on the tubal mucosa. It seems probable that in many of these cases the peritoneal condition was primary and the adnexal involvement merely due to secondary extension. It was very noticeable that all the cases in group one occurred in patients under thirty years of age, and were often accompanied by an infantile condition of the genitals, suggesting the possibility of a congenital affection, or at least of a congenital tendency, or else that the tuberculosis settled here, owing to the imperfectly developed genital organs offering a *locus minoris resistentiæ*. The cases in group two, on the other hand, occurred about evenly before and after thirty years of age. In many of the cases in group one the adnexal tuberculosis had evidently existed for a considerable time without any extension to the peritoneum, so that Meyer does not think one should feel forced to operate as soon as a diagnosis of tuberculosis of the tubes has been made for fear of its extending to the peritoneum, but considers that attempts at non-operative treatment should be made first. When driven to operation, it should, in view of the youth of most of these patients, be the aim of the surgeon to preserve an ovary, or at least a part of one, although this may necessitate a radical operation later on. Although the cases in group two have practically no pain, they do have a marked and increasing swelling of the abdomen, and therefore, as a rule, come to operation sooner than those of group one, in which latter pain is usually present; this pain is in no wise characteristic, however, and is often considered by the patients as due merely to slight menstrual disorders. These pains may occasionally start very suddenly, with peritonitic symptoms, and the diagnosis from appendicitis or ovarian cyst with a twisted pedicle be very difficult. Ten cases out of the 40 died, all more than two weeks after operation. The mortality was much higher in cases of peritoneal tuberculosis, in which the abdomen was merely opened and closed again, than in cases of adnexal disease, in which much more extensive operations were performed, showing that the character of the disease was a much more important factor in the mortality than the nature of the operation. The mortality was especially high in cases where fever was present before operation, so that Meyer considers this a grave prognostic condition. He also found a great tendency for wound suppuration to occur in feverish patients, and thinks that wounds in all tuberculous patients have a general tendency to heal poorly, the tuberculous process often extending to the wound surface, a condition which is sometimes favorably influenced by the action of direct sunlight. He also considers existing lung lesions a very grave complication, as they generally show a tendency to grow worse after operation, so that no operation should be undertaken in these cases without the most careful consideration.

OTOLOGY.

UNDER THE CHARGE OF

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A Foreign Body (Revolver Bullet) in the Temporal Bone Removed by Means of the Radical Operation.—WILHELM WALLER (*Monatsschr. f. Ohrenheilkunde*, 1911, p. 803). The patient was a woman, aged twenty-five years, who came under observation on account of a fetid discharge from the right ear of two years' duration, accompanied by severe tinnitus; the objective symptoms were those of a chronic suppurative middle-ear disease with the additional symptoms that pressure in the middle ear, incident to cleansing by means of the cotton-tipped probe, was accompanied by sharp contraction of the muscles supplied by the superior branch of the facial. Conservative treatment proving unavailing, the radical operation was decided upon, and the author was then first informed that the patient had attempted suicide two years previously by shooting herself in the right ear. Operation revealed two large pieces of metal lying close together in the antrum, the walls of the aditus being, furthermore, studded with small pieces of metal, the dura, which had been exposed over a considerable area, was normal, and the facial was bared to a short extent by absence of the wall of the nerve duct. The postaural wound was closed by primary suture, and, at the end of two and a half months, the cavity was healed and fairly epidermitized.

The Labyrinth Fistula Symptom.—G. ALAGNA (*La pratica otolaryngoiatrica*, 1911, No. 6). For the purpose of this test Alagna uses preferably the Siegle otoscope or the rarefactor of Delstanche, tightly inserted in the external auditory canal. The symptom is liable to be of negative value in young children and in adults with intact vestibular apparatus. During compression the nystagmus is directed toward the diseased, and during aspiration toward the sound side. The most frequent location of the fistulous opening is in the horizontal semicircular canal, and in cases of chronic suppurative middle-ear disease accompanied by loss of hearing, and in which the fistula symptom is positive, the radical operation, giving access to the horizontal canal and including the adequate opening of the labyrinth, is indicated. The fistula symptom has also been observed by Alagna in cases of non-suppurative labyrinthitis in hereditary syphilitics.

Examination of 200 Persons over Fifty Years of Age in Reference to Their Hearing Power.—TORRINI (*Monatsschr. f. Ohrenheilkunde*, 1911, pp. 2 and 3). The isolated observations of depreciation of hearing for certain classes of tones in persons over fifty years of age, and especially the results of tests concerning the upper tone limit, are substantiated in the carefully conducted investigation of Torrini,

who was able to determine a distinct depreciation both in the functions of sound transmission and of sound perception. In the speech tests the depreciation was especially notable for the whispered voice. In all cases in which the objective examination revealed the consequences of past inflammatory processes in the middle ear the depreciation of hearing was increased.

Suppurative Inflammation of the Middle Ear Relieved by Anti-syphilitic Treatment.—H. BOURGEOIS (*Annales du Maladie de l'oreille, etc.*, June, 1911). In this paper Bourgeois mentions the lack of precision in the determination of the immediate etiology as compared with the cases of grave impairment of hearing in the non-suppurative aural manifestations of syphilitic disease. While otorrhea is a frequent accompaniment of an aural lesion in hereditary syphilis, it appears usually as a sequence of pharyngeal ulceration, and develops as the result of a secondary infection of the buccal and pharyngeal mucosa, and general treatment is usually ineffectual. The case reported, however, would seem to demonstrate the possibility of the existence of middle-ear disease, of syphilitic origin, amenable to constitutional treatment—a woman, aged forty years, with a suppurative disease of the middle ear, insidious in its development and indolent in its progress, subjected to the usual local treatment for a period of three months without amelioration, but healing at the end of ten days of mixed treatment. The distinctive characteristics of the suppurative middle-ear disease of syphilitic origin are its indolence and the multiplicity of the perforations, as in tuberculosis, but lacking the excessive discharge, the rapidity of progress, and the extent of destruction characterizing the latter disease.

Operation for the Relief of Intense Labyrinthine Vertigo.—MATTE (*Archivf. Ohrenheilk.*, Band lxviii, Heft 3 and 4), in a previous communication, gave two reasons for operation upon the non-suppurative labyrinth, where other remedial measures had failed of effect, namely, unbearable subjective noises and unbearable incapacitating dizziness of labyrinthine origin, and in the present communication cites a case in support of his proposition. Thirteen years before his admission to hospital under Matte's observation, the patient had received a severe blow on the left side of the head, followed by unconsciousness and severe hemorrhage from the mouth, the nose, and the left ear; in the course of a few weeks, however, he had so far improved as to resume his usual farming work, but with a total loss of hearing in the left ear. Seven years later the patient began to have recurrent attacks, with sudden onset, of vertigo, nausea, and vomiting; these attacks sometimes lasted from one to three days, including the subsequent prostration, and later, from one to two weeks. At the end of two years the patient had become physically weakened and mentally depressed, and an exact determination of his static and auditory condition was only measurably attainable. The left drum-head was largely cicatricial, the malleus deeply retracted, and the patient complained, in addition to the sense of instability, of a constant high-pitched subjective noise accompanied at times by a deep-toned pulsatory murmur. In view of the long period since the original injury, thirteen years, and the increasing

severity of the labyrinth symptoms, operation was decided upon and effected postaurally, with removal of the cicatricial drumhead and the major ossicles, broad chiselling of the lateral wall of the epitympanic space, and opening into the labyrinth above and below the facial nerve, with subsequent curettage of the labyrinth interior; the canal was then divided medially, the resultant flaps secured in place by gauze, and the postaural wound closed by suture. The healing of the wound progressed without incident, one month after operation there was occasional subjective noise but no vertigo, and there had been no recurrence up to the time of the last report, a period of two years, but there was a mildly persistent, high-pitched, metallic subjective noise, more constant than in the period immediately following operation, and increasing in intensity and in depth of tone coincidently with over-excitement or overexertion.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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A New Pasteur Institute.—Some of our readers may not yet be aware that a splendid Pasteur Institute has just been opened in Algeria. In 1894 the Algerian Government began this work, and on a comparatively small but useful scale carried on protective work in human and veterinary disease. In 1909 a large sum of money was set apart by the Algerian Government, and Professor Calmette was intrusted with the direction of the construction of the new Institution, which now takes its place among the splendid laboratories of the world. A staff of eleven workers is already in charge of departments of Medical Bacteriology, of Agricultural Bacteriology, of Veterinary Medicine, and of Rabies. In the vicinity are two annexes, one of which is devoted to protection against rabies, and the other to veterinary pathology and the preparation of sera.

The Chemistry of the Cell.—In the symposium upon the chemistry of the cell, held under the auspices of the Columbia University Biochemical Association in February, 1911, some extremely useful and pithy communications were made relative to our present knowledge of the cell, which contain some points that it may be useful to recapitulate. The series of papers appears in the *Biochemical Bulletin*, vol. i, No. 1, September, 1911. W. J. GIES points out the importance of intracellular water which is contained free in the cell, is subject to evaporation, diffusion, and dehydration and forms the general medium of exchange inside the cell and between the cell and its liquid environ-

ment. It is in relatively stable equilibrium with the water among the adjacent tissue-cells, the water in the circulation, and that in the secretions and excretions. When the cells are desiccated they may lose from 50 to 98 per cent. of their weight, and this water it is which lodges the soluble intracellular compounds, and which is therefore concerned in osmotic processes. Of the intracellular water which is not free, some unites molecularly with colloids in a way comparable to the water of crystallization. W. H. WELKER points out that incineration does not give an accurate estimation of the inorganic substances contained in the cell, and aqueous extraction also fails to be accurate by reason of the production of free inorganic molecules in the process. Most of the true saline material in the cell is in solution in the intracellular water, either as molecules or ions, and is liable to enter into osmotic action and into new chemical combinations. In addition there are numerous combinations made with organic substances, which combinations are essentially of two types—one relatively unstable, like glucose-sodium, or sodium proteinate, and the other relatively stable, such as the phosphoric acid radicals in lecithin, and the iron in nucleoprotein. Substances of the latter type do not readily undergo hydrolysis, while those of the former are apt to do so. Finally there are absorption products between intracellular inorganic substances and colloids. Referring to intracellular carbohydrates, E. D. CLARK indicates the widespread storage of glycogen in the liver, muscles, and to some extent in all animal cells and organisms. The blood receives a supply of glucose from the alimentary tract, and yet preserves a constant glucose content; the cells in turn obtain from the blood the glucose necessary for heat and certain protoplasmic combinations. Maltose exists as free sugar in the animal cell in small quantity, derived probably from glycogen, while lactose is a constituent of the mammary cells during lactation. Combined carbohydrates exist in the nucleoproteins and the glycoproteins, while special tissues contain special combinations, such as the cerebrogalactosides of the nervous system and substances, such as jecorin, found in the liver, heart-muscle, and elsewhere. Many of the intracellular carbohydrates are soluble in the cell water, and therefore can diffuse; and while relatively stable, they yet enter into various combinations with water, salines, other carbohydrates, lipins, and proteins. Lipins are organic "fatty" substances insoluble in concentrated neutral saline solutions, but soluble in hot alcohol or warm ether, or both; they are largely in the guise of "masked" fat combined with other protoplasmic substances. Complex lipins such as lecithin and cephalin may contain a considerable amount of inorganic substance linked with the fatty part, and combinations of lipins and amino-acids occur synthetically, doubtless quite comparable with combinations that exist in protoplasms. ROSENBLOOM, in reviewing the lipins, refers to the numerous compounds of lipins and proteids as seen in the vitellins and many combinations into which lecithins appear to enter. With the carbohydrates, too, both synthetically and in the cell, the lipins form compounds as they do also with alkaloids; it is, perhaps, to such a combination in the heart muscle cells that the efficacy of digitalis is due, and by similar combinations of lipins and toxins, venoms, etc., or a replacement of part of the lipins by the toxins that the effect of such poisons is brought about. The subject

of the intracellular proteins is more widely understood than is that of lipins, and W. H. EDDY reviews our knowledge of these bodies. From the albumins and globulins of the cytoplasm, and keratin, elastin, chitin, and gelatine in the cell membranes, we pass to the nucleoproteins of the nucleoplasm and of chromatin, the phosphoprotein of the nucleoli, of the linin, and of the centrosomes. These proteins have doubtless much in common, and the protein molecule is to be considered as manifesting basic and acidic side-chains at the same time, though in varying predominance. The basic (NH_2) chains predominate in the histones, the acidic (COOH) in the nucleoproteins, mucoids, etc., while there is a balance in the neutral albumins. These side-chains, too, of different natures, are concerned with the faculty of polymerization possessed by the protein molecules and allow the formation of a great variety of addition compounds; not only this, but they unite with one another, all of which possibilities point to the innumerable forms in which cell proteins exist and to the enormous numbers of relationships into which they can enter. As to the state in which proteins exist in the cell there is necessarily much doubt. Are proteid solutions actual solutions or only suspensions? We cannot tell, but we do know that the study of relatively simple substances like arsenious sulphide indicates that it can exhibit every character of suspension, colloidal solution, and crystalloidal solution, so that it may almost be predicted that the time will come when colloid and crystalloid states will be considered as merely modifications dependent on differing size of molecules. The process of adsorption, by which combination of salts and proteins occurs, may be something different, on the one hand, from suspension, and on the other, from solution and chemical union; it may be that there is an adsorptive affinity comparable, in a less perfected degree, to chemical affinity. Intracellular enzymes, dealt with by A. P. LOTHROP, constitute a very difficult subject. Colloidal in nature, they are prone to be impure by reason of their adsorption compounds. While there is much evidence in favor of their protein nature, it is not yet definitely determined that they are proteins; cellular in origin, most enzymes exert their activity in cells, and most intracellular biochemical change is probably due to their activity. This does not apply to the so-called secretion enzymes, which are extracellular in their action. The imperfection of our knowledge of the intracellular enzymes is largely due to the very fact that their existence is closely connected with the cell activity and that they are thus difficult to extract. Without going further than to say that like toxins, the enzymes stimulate the tissues to the formation of antibodies, it may be said that in enzyme action we have probably the most potent factor in the interaction of particles of living matter, and that it supplies the connecting links between the various complex intracellular constituents that have been mentioned.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSON, 1927 Chestnut St., Phila., Pa., U. S. A.

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ORIGINAL ARTICLES

THE FUNCTIONAL DIAGNOSIS OF PANCREATIC DISEASE.¹

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IN the preface of his classical work on diseases of the pancreas, Oser² says that there is perhaps with no organ in the human body such a disparity between the height of its physiological importance and the low level of our clinical knowledge as with the pancreas. This statement is true today despite the advances that have been made during the fourteen years that have elapsed since Oser published his monograph.

It strikes one as strange that so little should be known about the diseases of an organ which plays such an important part in digestion and in intermediate metabolism as does the pancreas. It is the only gland which furnishes an enzyme for each of the three chief classes of organic foodstuffs. The activated proteolytic ferment, trypsin, breaks down the native proteins into simpler bodies than does the pepsin of the gastric juice. Steapsin splits the neutral fat of the food into glycerine and fatty acids. The third ferment, diastase, converts starch into sugar. The volume of pancreatic juice secreted in a day may amount to half a liter or more (Glaessner).

The importance of the pancreas in the metabolism of sugar is undoubted, although the way in which the pancreas acts is unknown.

¹ Read before the Section on General Medicine of the College of Physicians of Philadelphia, January 22, 1912. The investigations which furnished the material for this paper were made with the aid of grants from the Proctor Fund for the Study of Chronic Diseases.

² Die Erkrankungen des Pancreas, Nothnagel's Spec. Path. u. Ther., Vienna, 1898, 1
VOL. 143, NO. 3.—MARCH, 1912.

Amid much that is obscure one fact is clear. The total removal of the gland is always followed by diabetes which runs a rapidly fatal course.

It was formerly held that if the pancreatic juice was entirely excluded from the intestine a serious disturbance took place in the digestion of nitrogenous food, fats, and starches. This seems clearly proved by the experiments of Minkowski and Abelman, who found, after total extirpation of the pancreas in dogs, that very little of the fat and nitrogen was absorbed. In a few cases of extensive disease of the pancreas clinical observers had noted that the stools were fatty and contained many muscle fibers. Hence the conclusion that in pancreatic disease there was poor absorption of fat and nitrogen.

New studies beginning with those of Friedrich Müller³ threw doubt on the correctness of the accepted views. Müller showed clearly by careful chemical studies that steatorrhea was not pathognomonic of pancreatic disease, for fatty stools occurred in icterus. He claimed, moreover, that in pancreatic disease unassociated with jaundice there was no disturbance in the assimilation of fat and nitrogen.

Within the last few years several researches on the effect of tying the pancreatic ducts have been published in Europe. The results of these animal experiments supported the clinical observations of Müller. (Lombroso,⁴ Zunz and Mayer,⁵ Nicmann,⁶ and Fleckseder.⁷) Quantitative analyses of the feces seemed to show that little or no disturbance in the utilization of the fat and nitrogen of the food resulted from shutting out the pancreatic juice from the intestine. The statement made by Brugsch⁸ in a recent paper is in accord with the present views of A. Schmidt, Minkowski, and other German authorities. Brugsch said that the absence of pancreatic tissue and not the exclusion of the pancreatic juice from the intestine leads to disturbances in absorption. How a portion of the pancreas separated from the intestine by complete occlusion of the ducts can influence the digestion and absorption of food is not explained.

Observations made in our laboratory have shown the error of these views. We found that total exclusion of the pancreatic juice from the intestine always resulted in a great decrease in the assimilation of fats and proteins. As soon as the animal recovered from the operation and began to take food in quantity the stools became very large, soft, and fatty. There were usually several movements a day. On microscopic examination the feces were found to consist largely of undigested muscle fibers. In spite of ravenous appetites

³ Zeitsch. f. klin. Med., 1887, xii, 45.

⁴ Arch. f. exp. Path. u. Pharm., 1908, lix, 251.

⁵ Mém. couronnées et autres mém. p. p. l'Acad. Royale de Méd. de Belgique, 1906, xviii, 7.

Quoted by Hess.

⁶ Zeitsch. f. exp. Path. u. Ther., 1909, v, 466.

⁷ Arch. f. exp. Path. u. Pharm., 1909, lix, 407.

⁸ Deutsch. med. Woch., 1909, xxxv, 2307.

the dogs lost weight rapidly. Since the publication of the paper of Pratt, Lamson, and Marks,⁹ additional experiments made by Dr. Murphy and me have yielded confirmatory results. It is a difficult matter to exclude all the pancreatic juice from the intestine, and failure to do so explains the results obtained by other investigators. In a search of the literature I found that Hess¹⁰ had clearly shown this in a paper which appeared a year before our work was published. His admirable studies, buried in an obscure journal, have not received the attention they deserve. In every instance in which we succeeded in separating the pancreas permanently from the intestine extreme atrophy of the gland occurred. Absence of marked atrophy and sclerosis as well as the good absorption of food prove that Lombroso, Nicmann, Fleckseder, and other experimenters did not shut out all the pancreatic juice from the intestine.

Disease of the pancreas is relatively common, but disease of the pancreas with total exclusion of the pancreatic juice from the intestine is rare. There are scarcely two dozen cases in the literature in which the symptoms noted in our dogs, after total occlusion of the pancreatic ducts, were present.

In the clinical study of pancreatic disease it will be important to recognize, if possible, a diminution of pancreatic secretion as well as its total suppression.

Our experiments on dogs showed that the disturbance in absorption is slight when a small amount of functioning pancreas is left in connection with the intestine. In one dog Dr. Murphy separated the entire pancreas from the duodenum except for a wedge-shaped piece 1 cm. in length in the centre of which was the main pancreatic duct. The dog recovered rapidly from the operation. When fed on meat he had only one stool of moderate size daily. There was no fat visible on naked eye examination and no fat-droplets were seen with the microscope. The feces usually contained quite a large number of muscle fibers, with striations well preserved. The animal lost weight rapidly until fresh pancreas was added to his food. The operation was performed on March 16, 1910. The stools did not become fatty until the following November. The dog died on December 1, and the portion of pancreas that had been left connected with the intestine at the operation was reduced to a small strand of dense fibrous tissue. In another animal a small portion of the pancreas remained functioning after the operation. The stools were rather large, but well formed. A good many muscle fibers were present in the feces, but no apparent excess of fat. At the autopsy there was found a nodule of pancreatic tissue about 2 cm. in size, which contained acini and islands of Langerhans. Dr. Spooner demonstrated the presence of trypsin in the duodenal contents. In both of these animals the decreased

⁹ Trans. Assoc. Amer. Phys., 1909, xxiv, 266.

¹⁰ Medizinisch-Naturwissenschaftliches Archiv, 1908, i, 161.

pancreatic secretion was recognized by the presence of many muscle fibers in the stool, not by any excess of fat.

In the clinical study of cases of suspected pancreatic disease it is helpful to use the test diet of Adolf Schmidt. I have used it in my metabolism studies on patients during the past four years as well as in the routine examination of patients presenting symptoms of intestinal disease. This standard diet contains a very small amount of waste material. This is an important matter when a careful examination of the feces is to be made for the presence of undigested ingredients of the food. I have had no difficulty in inducing patients to follow this diet for the required period of three days. Sometimes, however, patients have refused to take the entire quantity of food prepared for each meal. Instead of following the original plan of giving five meals daily I have usually given the total amount of food in three meals. If this standard diet is used the results of absorption studies, as well as of the simpler clinical examinations, made by different investigators can be readily compared. Therein lies the great advantage of the Schmidt test-diet over similar ones that might readily be devised.

The form of test diet I have used is that given in the English translation of Schmidt's *Test Diet in Intestinal Diseases*, Philadelphia, 1906. It consists of "1.5 liters milk, 100 grams zwieback, 2 eggs, 50 grams butter, 125 grams beef, 190 grams potatoes, and gruel of 80 grams oatmeal. It contains about 102 grams albumin, 111 grams fat, 191 grams carbohydrates, or a total of 2234 calories."

In the morning: 0.5 liter milk (or, if milk does not agree, 0.5 liter cocoa prepared from 20 grams cocoa powder, 10 grams sugar, 400 grams water and 100 grams milk) and 50 grams zwieback.

In the forenoon: 0.5 liter oatmeal gruel (made from 40 grams oatmeal, 10 grams butter, 200 c.c. milk, 300 c.c. water, 1 egg; strained).

At noon: 125 grams chopped beef (raw weight), broiled rare with 20 grams of butter, so that the interior will still remain raw, and 250 grams potato broth (made of 190 grams mashed potatoes, 100 c.c. milk, and 10 grams butter).

In the afternoon: As in the morning.

In the evening: As in the forenoon.

In the recognition of severe pancreatic disease there is no single symptom of greater significance than bulkiness of the stools. This is a diagnostic sign to which Oser,¹¹ Musser,¹² and others have called attention. Much information can often be gained from the weight of the dried stools, and this can be ascertained even when facilities are not available for exact chemical analyses. All that is necessary in addition to scales for weighing is a water bath and a ventilating hood. With pancreatic juice absent from the intestine,

¹¹ Die deutsch. Klinik, Berlin, 1901, v, 165.

¹² Trans. Assoc. Amer. Phys., 1906, xxi, 346.

not only are the stools voluminous, but the dried residue is much in excess of the normal.

In a series of 6 healthy individuals placed on the test diet for three days, Schmidt¹³ found the average weight of the dried feces to be 54.3 grams. The maximum was 62 grams and the minimum 45 grams.¹⁴ I found in a case of obstructive jaundice associated with malignant disease of the pancreas that the weight of the dried feces was 419 grams in one metabolism period of three days, and 355 grams in another. In a patient with chronic fatty diarrhea and glycosuria without icterus the feces weighed 438 grams.

The increase in weight of the feces which results from shutting off the pancreatic juice from the intestine was well shown in our animal experiments. In a preliminary absorption test with the dog in normal condition the weight of the dried food in a period of three days was 624 grams, and the weight of the feces 140.4 grams. In a metabolism experiment of the same duration begun five days after separating the pancreas from the duodenum the weight of the dried food was reduced to 416 grams and that of the feces increased to 302.7 grams.

In none of the cases studied by Schmidt¹⁵ was such a marked increase in weight of the feces observed as in our 2 cases of pancreatic disease. The average weight of the feces in 5 cases of "fermentative dyspepsia" reported by him was 127.4 grams; the average in "gastrogenous diarrhea" with achylia was 98.9 grams. His highest figures were in obstruction of the common bile duct, where the average weight was 175.6 grams, and the maximum 215.4 grams. There are no observations on cases of obstruction of the pancreatic ducts given by Schmidt. It seems to me that the possibility of shutting off the pancreatic secretion by an obstruction in the lower part of the common bile duct should be recognized. This may be the explanation of the heavy weight of the feces in 2 of his cases. It would be interesting to know if an obstruction high up in the common bile duct is associated with less disturbance of assimilation than one at the diverticulum of Vater. Unfortunately we have no information on this point.

MACROSCOPIC EXAMINATION OF THE FECES. The light color of the feces is the most important sign of pancreatic disease brought out by the naked eye examination. This is due to the presence of fat, and if the amount of fat is large the stools become almost white. As the stools in icterus are also fatty, it may be necessary to make use of Schmidt's corrosive sublimate test for bile pigment in order to make sure that the pale color of the stools is not due in part to absence of hydrobilirubin. If fat crystals are present in large numbers they give to the feces a metallic lustre like that of

¹³ Die Faeces des Menschen, Dritte Auflage, Berlin, 1910, p. 17.

¹⁴ These figures of Schmidt are based on his original test diet, number II, which contains 1½ eggs and 20 grams more of sugar and 30 grams less of butter than the diet I employed.

¹⁵ Loc. cit.

aluminum. When large amounts of fat were given to our dogs with obstructed pancreatic ducts they passed yellow masses of pure fat which looked like melted butter. I have seen only one patient whose dejections contained similar collections of macroscopic fat. With a diet rich in fat, Tileston¹⁶ found masses of fat frequently in the stools of pancreatic disease. It should be borne in mind that fatty stools also occur in other conditions, chief of which are jaundice, already mentioned, diseases of the intestinal wall, and tabes mesenterica. Bits of muscle tissue, large enough to be easily recognized on inspection of the stools, were not found in our cases, and they were rarely seen in the feces of dogs after shutting out the pancreatic juice from the intestine.

MICROSCOPIC EXAMINATION OF THE FECES. The fat appears in the form of droplets, needle-crystals, and as structureless plates or flakes. The most trustworthy sign of the lack of pancreatic juice in the intestine is the presence of large numbers of yellow muscle fibers with sharp edges and with striations well preserved. They may be so numerous as to cover the entire field of the microscope when a low power is used.

To the pathological condition characterized by the presence of a large number of muscle fibers in the stool, Ehrmann¹⁷ has recently given the name creatorrhea. Although a small number of undigested muscle fibers may be present in the stools in other conditions, especially in diarrhea, a well marked creatorrhea has never been observed in cases in which pancreatic insufficiency has been definitely excluded. The presence of numerous muscle fibers in the stools was recognized by Friedreich nearly forty years ago to be a valuable diagnostic sign of pancreatic disease.

ABSORPTION OF FAT AND NITROGEN. In our dogs, as I have already stated, we found that shutting off all the pancreatic juice produced a great diminution in the absorption of both nitrogen and fat. This is shown in the following table:

TABLE I.

		Absorption in per cent. of		Notes.
		N.	Fat.	
Dog II.	Experiment 1	22.2	11.3	Pancreas separated from duodenum.
"	" 2	62.1	48.5	Pankreon given.
Dog III.	Experiment 1	88.5	92.2	Before operation.
"	" 2	23.7	10.0	After excluding pancreatic secretion from intestine.
Dog IV.	Experiment 1	92.4	91.4	Before operation.
"	" 2	31.7	44.6	After excluding pancreatic secretion from intestine.
"	Experiment 3	47.8	63.4	
"	" 4	31.4	76.6	
Dog V.	Experiment 1	32.1	31.0	After excluding pancreatic secretion from intestine.
"	" 2	61.7	4.8	
"	" 3	42.4	20.1	
"	" 4	56.0	44.0	Holadin given.

¹⁶ Albany Med. Ann., 1909, xxx, 619.¹⁷ Zeitsch. f. klin. Med., 1910, lxi, 331.

The clinical study of the metabolism of man in disease began with Friedrich Müller's¹⁸ researches on icterus, published in 1887. In 3 cases of pancreatic disease he determined the amount and composition of the fecal fat. He concluded that the pancreatic juice could be excluded from the intestine without producing any quantitative change in the fecal fat. Autopsies were held in 2 of his cases. At that time it was not known that the human pancreas is regularly provided with two ducts. In the protocols no mention is made of the duct of Santorini. The entrance of pancreatic juice into the intestine through the accessory duct would explain Müller's findings. I analyzed the intestinal contents obtained at autopsy in a case of adenocarcinoma of the head of the pancreas, in which the duct of Wirsung was obliterated, but the duct of Santorini was patent. There was also obstruction of the common bile duct. The feces were not bulky and there was only 28.8 per cent. of fat in the dried residue.

In a number of cases of pancreatic disease metabolism studies have shown a great interference with the absorption of fat and nitrogen. Morrison and I made a metabolism experiment on a patient presenting the typical symptoms of total obstruction of the pancreatic ducts. There was no jaundice. It was found (Table II) that 58.9 per cent. of the fat of the food was excreted in the feces. The percentage of nitrogen unabsorbed was 50.9 per cent. Normally not over 5 or 10 per cent. of the fat or nitrogen of the food is lost in the feces.

TABLE II.

McC.	Three days' experiment, October 20 to 22, 1908.
	Weight of dried food 1297.5 grams. (Schmidt test diet.)
	Weight of dried feces 438.0 grams.
	Percentage of fat in food, 35.16; amount, 456.2 grams.
	Percentage of fat in feces, 61.3; amount, 268.5 grams.
	Percentage of nitrogen in food, 3.86; amount, 50.08 grams.
	Percentage of nitrogen in feces, 5.82; amount, 25.49 grams.
	Fat unabsorbed, 58.9 per cent.
	Nitrogen unabsorbed, 50.9 per cent.

In a metabolism experiment on a patient with cancer of the pancreas and obstructive jaundice, Spooner and I found that 79.9 per cent. of the fat of the food was excreted in the feces and 34.8 per cent. of the nitrogen.

Vaughan Harley¹⁹ reported a case of probable obstruction of the pancreatic ducts without jaundice, in which there was a fat loss of 73.1 per cent. In a case of cirrhosis and atrophy of the pancreas, combined with cirrhosis of the liver, Weintraud²⁰ found a fat loss

¹⁸ Loc. cit.²⁰ Die Heilkunde, 1898, iii, 68.¹⁹ Jour. Path. and Bact., 1895, iii, 245.

of 25.2 per cent.; Deucher,²¹ in cancer of the pancreas, found fat losses of 82.9 per cent. and 52.6 per cent.; Brugsch and König,²² in a case of abscess of the pancreas, 59.7 per cent. (absorption experiment of only one day's duration). Glaessner and Siegel,²³ in a case of atrophy of the pancreas due to a calculus, found a fat loss of 56.1 per cent.; Gigon,²⁴ in a case of pancreatic calculi with obstruction of the ducts, a maximum fat loss of 47.4 per cent. and a minimum of 13.5 per cent.; Ehrmann,²⁵ in atrophy of the pancreas 50.2 per cent.; Tileston,²⁶ in 5 cases of cancer of the pancreas with icterus, fat losses of 75.6 per cent., 68 per cent., 52.6 per cent., 45.6 per cent., 49.1 per cent.

In Harley's case there was a nitrogen loss of 40 per cent.; Weintraud found a nitrogen loss of 60.6 per cent.; Deucher, 29.6 per cent. in one case and 19 per cent. in the other. Glaessner and Siegel, 41.5 per cent.; Gigon, 24.7 per cent.; and Ehrmann, 42.8 per cent.; Tileston, in 3 cases, 19.8 per cent., 14.5 per cent., and 21.1 per cent. Brugsch²⁷ found an average fat loss of 45 per cent. in 3 cases of icterus, but the nitrogen loss averaged only 11 per cent. If 50 per cent. or more of the fat and 25 per cent. of the nitrogen of the food are recovered from the feces the conclusion is warranted that pancreatic insufficiency exists.

COMPOSITION OF THE FECAL FAT. Müller observed that the feces contained a larger percentage of unsplit fat, that is, of neutral fat, in his cases of pancreatic disease than in other conditions studied. Zoja²⁸ asserted that a low percentage of soaps was of diagnostic value. Fitz,²⁹ in 1903, collected 11 cases from the literature in which an analysis of the fecal fat had been made. While in health, from 20 to 30 per cent. is in the form of neutral fat, in 9 out of 11 cases of disease of the pancreas the percentage of neutral fat was increased.

Since 1904 I have made analyses of the fecal fat in 7 cases of undoubted pancreatic disease. The fat extractions were made according to Rosenfeld's³⁰ method. In the determinations of the neutral fat, fatty acids, and soaps, Fr. Müller's³¹ procedure was followed. The results are given in the following table.

²¹ Korrespondenz-Blatt f. Schweiz. Aerzte, 1898, xxviii, 321.

²² Berl. klin. Woch., 1905, xlii, 1606.

²³ Ibid., 1904, xli, 440.

²⁴ Zeitsch. f. klin. Med., 1907, lxxiii, 420.

²⁵ Loc. cit.

²⁶ Trans. Assoc. Amer. Phys., 1911, xxvi, 526.

²⁷ Zeitsch. f. exper. Path. u. Ther., 1909, vi, 326.

²⁸ Morgagni, 1899. Ref. in Centralbl. f. inn. Med., 1899, xx, 1261.

²⁹ Trans. Cong. Amer. Phys. and Surg., 1903, vi, 36.

³⁰ Zentralbl. f. inn. Med., 1900, xxi, 833.

³¹ Loc. cit.

TABLE III.—Analyses of Feces in Disease of the Pancreas.

CASE I.—Mrs. H. Cancer of pancreas, with occlusion of pancreatic ducts; glycosuria; obstructive jaundice. Autopsy.

	Per cent. of nitro- gen in feces.	Per cent. of fat.	Per cent. of neu- tral fat.	Per cent. of fatty acids.	Per cent. of soaps.
Stool of January 28	2.0	49.7	22.5	58.7	18.8
Stool of February 22	5.0	62.8	29.1	63.2	7.7

CASE II.—B. Cancer of pancreas; transitory glycosuria; obstructive jaundice. Diagnosis confirmed by operation.

	Per cent. of nitro- gen in feces.	Per cent. of fat.	Per cent. of neu- tral fat.	Per cent. of fatty acids.	Per cent. of soaps.
	6.0	72.8	39.7	50.5	9.8

CASE III.—Mrs. C. Cancer of pancreas; shortly before death on October 29 stools became soft and fatty. Autopsy. Obstruction of duct of Wirsung; accessory duct not found; partial obstruction of common bile duct.

	Per cent. of nitro- gen in feces.	Per cent. of fat.	Per cent. of neu- tral fat.	Per cent. of fatty acids.	Per cent. of soaps.
October 9. Small clay-colored stool. It did not look fatty .	4.29	52.5	37.1	37.3	25.6
First stool that looked fatty .	3.0	63.3	14.0	30.9	55.1

CASE IV.—S. Cancer of head of pancreas; slight jaundice. Diagnosis confirmed by tissue removed at operation.

	Per cent. of nitro- gen in feces.	Per cent. of fat.	Per cent. of neu- tral fat.	Per cent. of fatty acids.	Per cent. of soaps.
	4.8	66.1	30.7	44.8	24.5

CASE V.—M. Cancer of pancreas; duct of Wirsung obliterated; duct of Santorini patent; partial occlusion of the common bile duct.

	Per cent. of fat.	Per cent. of neu- tral fat.	Per cent. of fatty acids.	Per cent. of soaps.
	28.8	3.9	18.2	77.9

CASE VI.—McC. Clinical diagnosis: Obstruction of pancreatic ducts. No autopsy.

	Per cent. of nitro- gen in feces.	Per cent. of fat.	Per cent. of neu- tral fat.	Per cent. of fatty acids.	Per cent. of soaps.
	5.8	61.3	56.6	37.4	6.0

CASE VII.—G. Cancer of pancreas; complete occlusion of common bile duct; primary cancer of stomach. Operation.

	Per cent. of nitro- gen in feces.	Per cent. of fat.	Per cent. of neu- tral fat.	Per cent. of fatty acids.	Per cent. of soaps.
	4.3	70.4	41.8	37.5	20.7

In all but one of these cases steatorrhea occurred. The percentage of fat ranged from 28.8 to 72.8, while normally the feces contain less than 25 per cent. In 4 of the 7 cases there was an increase in the neutral fat, but not sufficiently great to be of distinct diagnostic value. A very low percentage of soaps was found in 3 of the 7 cases.³²

It is evident from these analyses that additional methods of examination must be used in order to make a positive diagnosis of pancreatic disease.

EFFECT OF ADMINISTERING PANCREAS. The feeding of raw pancreas and pancreatic preparations causes an increased absorption of fat and nitrogen when there is a lack of pancreatic juice in the intestine. In our dogs with pancreatic juice absent from the intestine the feeding of fresh pancreas was followed by a great decrease in the loss of fat and nitrogen. Pancreatic preparations produced a less marked improvement in absorption, but in one experiment the addition of pankreon to the food reduced the fat loss from 88.7 per cent. to 51.5 per cent., and the nitrogen loss from 77.8 to 47.9 per cent.

It has been suggested by von Noorden, Fitz, and others, that in cases of suspected pancreatic disease the administration of raw pancreas or pancreatic extracts would be of diagnostic value. In a case of fatty diarrhea, apparently not due to disease of the pancreas, Morrison and I found in a five days' metabolism experiment a fat loss of 23.4 per cent., and a nitrogen loss of 16 per cent. Pankreon was given in large doses for a second period of four days, during which the fat loss was 25.7 per cent., and the nitrogen loss 15.3 per cent. These figures show that the pankreon had no effect on the absorption of food, and hence the experiment supports the view that the fatty diarrhea was not of pancreatic origin.

The results of absorption experiments made by a number of investigators have been collected by Tileston.³³ They show that pancreas and pancreatic preparations often decrease greatly the loss of nitrogen and fat in the feces. Sometimes, however, the effect of pancreatic preparations is so slight that it cannot be recognized unless an absorption experiment is performed.

A number of functional tests for the recognition of pancreatic insufficiency have been employed during recent years, and methods devised for demonstrating the enzymes of the pancreas in the feces, gastric contents, and urine.

GLUTOID CAPSULE TEST. This was introduced by Sahli³⁴ in 1897. Gelatine capsules containing salol or iodoform are hardened

³² In dogs the fats were as well split after shutting out the pancreatic secretion as they were in normal dogs, and the percentage of soaps was not decreased (Pratt, Lamson, and Marks, Trans. Assoc. Amer. Phys., 1909, xxiv, 266).

³³ Trans. Assoc. Amer. Phys., 1911, xxvii, 537.

³⁴ Deutsch. med. Woch., 1897, xxiii, 6; Deutsch. Arch. f. klin. Med., 1898, lxi, 475.

in formalin. This renders them resistant to gastric digestion, but they are dissolved readily by the pancreatic juice. The capsules I used contained salol, which is broken down in the intestine and excreted in the urine as salicyluric acid. Its presence is recognized by the violet color produced by adding to the urine a few drops of a solution of ferric chloride. Normally the reaction is obtained within five hours. The test would probably have been more widely used if Sahli had disclosed his method of preparing the capsules. They are made and sold by Fr. Hansmann, St. Gallen, Switzerland. My observations are based on tests made with the original capsules. An attempt to make glutoid capsules in our laboratory by placing gelatine capsules in 10 per cent. formalin for varying lengths of time ended in failure. I tested the imported capsules in artificial digestive fluids, and confirmed the claim of Sahli that they would resist gastric digestion and yet dissolve readily in pancreatic juice. Sailer³⁵ has found that satisfactory glutoid capsules can be made by immersing ordinary gelatine capsules in pure formalin for three minutes.

The test has few friends, and does not seem to be often employed at the present time. Schmidt's pupil, Wallenfang,³⁶ found the reaction delayed in 4 out of 8 healthy individuals. Schmidt says that it is of negative value, for if the reaction occurs within the normal time limit he holds that pancreatic disease can be definitely excluded. This statement, however, cannot be accepted, as the following observation shows. On February 22 I gave Mrs. H. two glutoid capsules, each containing 0.5 grams of salol. They were administered with an Ewald breakfast at 8 A.M. Urine voided at 12 o'clock contained salicyluric acid. The patient died on March 5, and a cancer of the head of the pancreas was found apparently occluding both ducts. If there is motor insufficiency of the stomach the test may be retarded. In one of my patients in whom a gastro-enterostomy had been performed the reaction was delayed many hours. Operation revealed a normal pancreas. The stools were negative. Attention has been called by Fromme³⁷ to the importance of ruling out gastric stasis in cases in which the glutoid capsule test indicates pancreatic disease.

When there is total absence of pancreatic juice from the intestine it is possible that a delay in the reaction always occurs. In a dog with the pancreas completely separated from the duodenum the reaction after the administration of the capsule was delayed nearly twenty-four hours, and then only a trace of salicyluric acid was found in the urine. In another dog in which a small bit of the pancreas, 1 cm. in size, was left connected with the main pancreatic duct, the reaction was not definitely retarded. I used capsules of medium

³⁵ AMER. JOUR. MED. SCI., 1910, cxi, 330.

³⁷ Münch. med. Woch., 1901, xlviii, 591.

³⁶ Inaug. Dissert., Bonn, 1903, p. 18.

hardness, but Sahli³⁸ now states that capsules of maximum hardness should be employed for diagnostic purposes. I found the reaction delayed, however, with the softer capsule in a case in which the presence of trypsin was demonstrated in the gastric contents after an oil breakfast.

SCHMIDT'S CELL NUCLEI TEST. The observation made by Schmidt,³⁹ that cell nuclei are digested only by the pancreatic secretion, is the physiological basis of the test. The method has been assailed on theoretical as well as on practical grounds. Brugsch⁴⁰ and his pupil Hesse⁴¹ have been the chief opponents of the method, but they have failed to prove that it is untrustworthy, and Schmidt's assertion that the gastric juice does not act upon cell nuclei seems to be true. Strauch,⁴² working in Abderhalden's laboratory, showed that pure pancreatic juice completely dissolved the cell nuclei in six to eight hours, pure intestinal juice (erepsin) and pure gastric juice, on the contrary, did not digest them.

I found in a dog with complete pancreatic achylia, produced by separating the pancreas from the duodenum, that the cell nuclei were not digested. The gastric juice was normal, and there was no disease of the intestine. Thus clear evidence was presented by this experiment that the normal secretions of stomach and intestine were unable to digest the cell nuclei.

Raw beef containing a fair amount of fibrous tissue is cut into cubes measuring about 0.5 cm. in size. These are hardened in alcohol, and placed in small bags made of silk gauze. They should be immersed in water for several hours before using. The bags are recovered from the stools, and the meat cubes examined for the presence of nuclei after paraffin sections have been prepared. The test is positive if the nuclei are preserved and take the stain, negative if the nuclei are digested. Einhorn⁴³ has used thymus gland instead of beef. This modification appears to be a distinct improvement, but I have had no personal experience with it.

Recently Kashiwado,⁴⁴ a pupil of Schmidt, has simplified the nucleus test. By gastric digestion the nuclei of the thymus gland are isolated. The nuclei are then stained with hematoxylin, and a powder prepared, composed of equal parts of lycopodium and nuclei. Two capsules, each containing 0.25 gram of the mixture, are administered after dinner or supper. If the nuclei are not digested they are easily recognized in the stools.

I have not observed a definite case of pancreatic insufficiency in which the nucleus test was negative. The value of the test is

³⁸ *Diagnostic Methods*, second English edition, Philadelphia, 1911 p. 606.

³⁹ *Verhand. d. Kong. f. inn. Med.*, 1904, xxi, 335.

⁴⁰ *Deutsch. med. Woch.*, 1909, xxxv, 2307; *Zeitsch. f. exper. Path. u. Ther.*, 1909, vi, 326.

⁴¹ *Zeitsch. f. exper. Path. u. Ther.*, 1909, vii, 91; *Deutsch. med. Woch.*, 1910, xxxvi, 121.

⁴² *Deutsch. Arch. f. klin. Med.*, 1910, ci, 128.

⁴³ *Arch. f. Verdauungskrank.*, 1907, xiii, 475.

⁴⁴ *Deutsch. Arch. f. klin. Med.*, 1911, civ, 534.

impaired by the fact that the meat cubes must remain in the intestine not less than six nor more than thirty hours. If the period is too short the nuclei are undigested by normal pancreatic juice. Putrefaction may cause the disappearance of the nuclei if the meat cubes remain more than a day in the intestine. In one of my cases the silk bags were recovered in the feces five days after they were taken into the stomach.

The preservation of the nuclei, with the test properly carried out, does not necessarily imply complete absence of the pancreatic secretion. In a case of fatty diarrhea with achylia gastrica the nuclei were not digested, but Spooner and I demonstrated trypsin in the stomach by Vollhard's method. If with the nuclei test one can recognize cases in which there is a deficient secretion of pancreatic juice, the value of the method will not be diminished but enhanced. As already stated, there are few cases of pancreatic disease in which total absence of pancreatic secretion occurs, and these are readily diagnosticated.

In 1906 Schmidt⁴⁵ described cases in which he maintained there was functional pancreatic achylia. I have seen cases of the type he described, but I believe that, as in the one just mentioned, there is a deficiency of the pancreatic juice (hypochylia) rather than total suppression of the secretion. The absorption of fat and nitrogen may be so good that the stools present no suggestion of pancreatic disease and yet the cell nuclei may remain undigested as in a case reported by the late Dr. Steele,⁴⁶ of Philadelphia. Three times the test was repeated, and each time the cell nuclei were found intact. In the light of present knowledge it seems probable that this was an instance of functional pancreatic hypochylia. This view is strengthened by the fact that there was an absence of gastric secretion in his case.

DEMONSTRATION OF TRYPSIN IN THE STOOLS. *The Serum Plate Method.* Müller and Schlect⁴⁷ found that trypsin would act upon the surface of a serum agar plate, producing small depressions. They demonstrated by this method the regular occurrence of trypsin in normal feces. The plates were kept at a temperature of 50° or 60° C., so that bacterial action was prevented. In several cases of primary and secondary disease of the pancreas trypsin was absent from the feces or greatly diminished. A number of investigators have found this method of value. It yielded positive results in 5 out of 6 cases of pancreatic disease examined by M. Hirschberg.⁴⁸

The Casein Method. Casein in alkaline solution is precipitated by acidifying with dilute acetic acid. When the casein is digested by trypsin the addition of acetic acid produces no clouding of the solution. This is the basis of a method introduced by Gross⁴⁹ for

⁴⁵ Deutsch. Arch. f. klin. Med., 1906, lxxxvii, 456.

⁴⁶ Trans. Assoc. Amer. Phys., 1906, xxi, 346.

⁴⁷ Deutsch. med. Woch., 1910, xxxvi, 1892.

⁴⁸ Münch. med. Woch., 1908, lv, 225.

⁴⁹ Arch. f. exper. Path. u. Pharm., 1907, lviii, 157; Deutsch. med. Woch., 1909, xxxv, 1706.

detecting the presence of trypsin. More than 200 stools were examined by him, and in all cases in which disease of the pancreas could be excluded a protein splitting ferment was present in the feces. A modification of Gross's method has been used by Dr. Spooner in our laboratory for estimating the amount of trypsin present in the feces. In one of our dogs with the pancreatic juice excluded from the intestine there was no splitting of the casein by the feces. This would indicate that erepsin was not present in sufficient amount normally to act upon the casein. The possibility that there was a diminished production of erepsin in the intestine of our dog, however, cannot be denied, although it seems improbable. Brugsch and Masuda⁵⁰ have concluded from their investigations that the strong splitting of casein produced by fecal extracts cannot be attributed to erepsin. Spooner and I, in a recent case of cancer of the pancreas, found that the power of the feces to digest casein was entirely lost. In a case of fatty diarrhea, probably due to pancreatic hypochylia, the amount of trypsin in the feces was greatly reduced. In this case the cell nuclei were not digested in Schmidt's beef-cubes, and after the administration of Sahli's glutoid capsules no reaction was obtained in the urine even at the end of twenty-four hours. That an absence of trypsin in the feces always indicates disease of the pancreas is doubtful. No trypsin could be demonstrated in the feces of one of the workers in our laboratory. Four tests were made during a period of ten weeks. He presented no symptoms of disease.

DEMONSTRATION OF TRYPSIN IN THE STOMACH CONTENTS. Boldyreff,⁵¹ in Pawlow's Institute made the important discovery that the feeding of a large amount of olive oil to dogs caused the regurgitation of pancreatic juice and bile from the duodenum into the stomach. Volhard⁵² and his pupil Faubel⁵³ were the first to use this method in the clinic. A breakfast, consisting of 200 c.c. of pure olive oil is given, or in place of the oil 250 c.c. of cream may be used.

As trypsin cannot be demonstrated in a strongly acid gastric juice, half a teaspoonful of magnesia should be given before breakfast and twenty minutes later, as suggested by Lewinski.⁵⁴ Some remove the stomach contents in half an hour, others at the end of forty-five minutes. Trypsin estimations can be made by Volhard's method or more easily by that of Gross.

Mahlenbrey⁵⁵ proved the presence of trypsin in the stomach contents of 38 out of 41 cases. This method has been utilized in

⁵⁰ Zeitsch. f. exper. Path. u. Ther., 1911, viii, 617.

⁵¹ Zentralb. f. Physiol., 1904, xviii, 457; Zentralb. f. Phys. u. Path. des Stoffw., 1908, iii, 209.

⁵² Münch. med. Woch., 1907, liv, 403.

⁵³ Beitr. z. chem. Phys. u. Path., 1907, x, 35.

⁵⁴ Deutsch. med. Woch., 1908, xxxiv, 1582.

⁵⁵ Zentralb. f. ges. Phys. u. Path. des Stoffw., 1909, iv, 643, 689.

the diagnosis of pancreatic disease by Volhard,⁵⁶ Lewinski,⁵⁷ Ehrmann,⁵⁸ and M. Hirschberg.⁵⁹

Spooner and I found trypsin in the stomach contents of a patient who had fatty diarrhea and achylia gastrica. The Schmidt nuclei test and the glutoid capsule test indicated pancreatic inactivity. Until the demonstration of trypsin in the oil breakfast the possibility of achylia pancreatica could not be excluded.

DEMONSTRATION OF TRYPSIN BY DUODENAL INTUBATION. Attention should be called to the ingenious method of obtaining pancreatic juice directly from the duodenum devised by Einhorn.⁶⁰ A gold acorn-shaped bucket, the size of a bean, is swallowed. Attached to the bucket is a strong silk thread, the free end of which, passing out of the patient's mouth is fastened around his neck or to his clothes. After time has elapsed for the bucket to enter the duodenum a catheter is passed along the thread and so guided into the duodenum. By means of a syringe it is then possible to aspirate the duodenal contents through the catheter. Gross⁶¹ has also invented a duodenal tube. Von Barth-Wehrenalp,⁶² by the use of Einhorn's bucket without the aspiration catheter was able to obtain pancreatic secretion in 55 per cent. of the cases he examined. Junghans⁶³ demonstrated the presence of trypsin in 30 out of 50 cases. The bucket was retained by his patients the entire night, while von Barth-Wehrenalp removed it at the end of three hours. Junghans obtained no better results when the duodenal tubes of Einhorn and Gross were used. Einhorn⁶⁴ has improved his method. In place of the duodenal bucket he has devised a duodenal pump consisting of a small perforated metal capsule communicating with a long thin rubber tube. By means of a syringe connected with the rubber tube the duodenal contents are aspirated.

DIASTASE IN THE FECES. Within the last two years a new laboratory test has been employed by a few investigators in the diagnosis of pancreatic disease which is full of promise. This is the quantitative determination of the diastatic ferment in the feces and urine. Strasburger⁶⁵ was the first to show that diastase was normally present in the stools of adults. Its occurrence in the feces of children had long been known. Strasburger thought the starch-splitting enzyme was a product of the intestinal secretion. Its clinical significance was not realized until Wohlgemuth proved that the diastase of the feces came chiefly from the pancreas. The original method of diastasimetry is that of Roberts. The one chiefly

⁵⁶ Loc. cit.

⁵⁷ Loc. cit.

⁵⁸ Loc. cit.

⁵⁹ Loc. cit.

⁶⁰ New York Med. Jour., 1908, lxxxvii, 1179; Arch. f. Verdauungskrank., 1909, xv, 727; Med. Rec., 1909, lxxvi, 595.

⁶¹ New York Med. Jour., 1910, xci, 77; Jour. Amer. Med. Assoc., 1910, liv, 1365.

⁶² Intern. Beit. z. Path. u. Ther. d. Ernährungstor., 1910, i, 530.

⁶³ Zentralb. f. Phys. u. Path. d. Stoffw., 1911, vi, 49.

⁶⁴ Med. Rec., 1910, lxxvii, 98; Jour. Amer. Med. Assoc., 1910, lv, 6.

⁶⁵ Deutsch. Archiv f. klin. Med., 1900, lxxvii, 238, 531.

used at the present time was introduced by Wohlgemuth.⁶⁶ It has been modified by Wynhausen⁶⁷ and Hawk.⁶⁸ Other methods are those described by Salkowski, E. Müller,⁶⁹ and Durand.⁷⁰

E. Müller, using his starch plates, found a very weak diastatic action of the stool in a case of complete occlusion of the ductus pancreaticus. Einrequez, Ambard, and Binet⁷¹ noted an absence of diastase in the feces of 2 cases of cancer of the pancreas. Wynhausen⁷² examined 4 cases of pancreatic disease (2 of cancer; 2 of hemorrhagic pancreatitis). In none of these were more than 30 diastase units in the stool, while normally an average of 500 units are found. Balint and Molnar⁷³ reported that in a case of cancer of the pancreas repeated examinations of the stool showed the total absence of diastase. Wynhausen,⁷⁴ in a more recent paper, states that in 12 cases of pancreatic disease confirmed by autopsy the method of Wohlgemuth yielded trustworthy results, not only in cancer of the pancreas, but in diffuse affections of the gland which did not involve the ducts.

DIASTASE IN THE URINE. The observation of Wohlgemuth⁷⁵ that the experimental occlusion of the main pancreatic duct in dogs is followed by a marked rise in the amount of diastase in the urine lead to the important discovery that in acute functional disturbances of the pancreas in man a similar increase in the diastase of the urine occurs. In 2 cases Wohlgemuth⁷⁶ obtained values of 625 and 1250, while the highest observed normally was 150 units. Hirschberg⁷⁷ found a large amount in 2 cases of acute pancreatitis, and Wynhausen in 2 cases of cancer of the pancreas. The increase is seen only in acute disease or at the onset of increased disturbance of function which may occur in a chronic disease.

LIPASE IN THE URINE. Opie,⁷⁸ in 1902, reported the occurrence of a fat-splitting ferment in the urine of a case of acute hemorrhagic pancreatitis. His test is open to criticism, because the possibility cannot be denied that the lipolytic action he observed was due to bacteria. Hewlett⁷⁹ has clearly demonstrated, however, that lipase appears in the urine of dogs after obstruction of the pancreatic duct, and during acute pancreatitis experimentally produced.

In 2 cases of acute pancreatitis in which I examined the urine I could find no fat-splitting ferment. I used the same method as did Opie, but added toluol to check the development of bacteria. In the new edition of his work on the pancreas, published in 1910,

⁶⁶ Biochem. Zeitsch., 1908, ix, 1.

⁶⁸ Arch. Int. Med., 1911, viii, 417.

⁷⁰ Arch. mal. app. digest., 1911, v, 76.

⁷² Berl. klin. Woch., 1910, lxvii, 478.

⁷⁴ Abstracted in Zentralb. f. inn. Med., 1911, xxxii, 818.

⁷⁵ Biochem. Zeitschr., 1909, xxx, 432.

⁷⁷ Loc. cit.

⁷⁸ Johns Hopkins Hosp. Bull., 1902, xviii, 117.

⁶⁷ Berl. klin. Woch., 1909, xlii, 1406.

⁶⁹ Zentralb. f. inn. Med., 1908, xxix, 385.

⁷¹ Sem. Méd., 1909, xxix, 13.

⁷³ Berl. klin. Woch., 1910, xlvii, 1623.

⁷⁶ Berl. klin. Woch., 1910, xlvii, 92.

⁷⁹ Jour. Med. Research, 1904, vi, 377.

Opie⁸⁰ records no additional cases either of his own or from the literature.

ETHEREAL SULPHATES IN THE URINE. Absence of pancreatic juice diminishes intestinal putrefaction because bacteria break down proteins less easily than they do the end-products of pancreatic digestion. Hence the claim has been made that in pancreatic disease the ethereal sulphates in the urine are decreased or absent. In the urine of a normal dog on a meat diet, I found the ratio of ethereal to preformed sulphates was 1 to 9. In a dog with pancreatic juice absent from the intestine the ratio was 1 to 21.6 on one day, and 1 to 23.5 on the following day. Rosenberg,⁸¹ after tying one or more of the pancreatic ducts in a dog found the ratio was 1 to 15.9. Gigon,⁸² in the urine of a patient with pancreatic calculi obtained a ratio of 1 to 39.3, while normally it is about 1 to 10. Le Nobel,⁸³ in a case of pancreatic disease found "no conjugate sulphuric acid." There was no decrease in the ethereal sulphates in a case of pancreatic insufficiency studied by Tileston.⁸⁴

DISTURBANCE OF THE INTERNAL FUNCTION OF THE PANCREAS. All the functional tests described thus far in this paper have dealt with the enzymes of the external secretion, and the symptoms due to their absence from the intestine.

In addition there is the internal function which controls in some way, quite unknown, the normal destruction of sugar in the body. In disease of the pancreas the limit of assimilation for carbohydrates may be greatly lowered even when spontaneous glycosuria does not occur. In my dogs with atrophy of the pancreas this diminished tolerance was a constant symptom.

ALIMENTARY GLYCOSURIA. If a lowered limit of assimilation for sugar exists in patients with suspected pancreatic disease, it can be discovered by giving 100 grams of glucose and testing the urine for sugar during the following twenty-four hours. The solution of glucose may be made more palatable by the addition of coffee. It is better to give the sugar after a light breakfast rather than on a fasting stomach.

In a collection I have made of 37 cases of pancreatic disease, carefully studied by functional methods, spontaneous glycosuria occurred 6 times and alimentary glycosuria 4 times. Only 2 of the 10 cases were cancer.

It is important to make repeated examinations of the urine as transitory glycosuria is a symptom that is frequently overlooked.

CAMMIDGE TEST. This so-called pancreatic reaction⁸⁵ seems to deserve the discredit into which it is falling. I think Wohlgemuth⁸⁶

⁸⁰ Diseases of the Pancreas, second edition, Philadelphia, 1910, p. 198.

⁸¹ Pflüger's Archiv, 1898, lxx, 404.

⁸² Deutsch. Archiv f. klin. Med., 1888, xliii, 280.

⁸³ Trans. Assoc. Amer. Phys., 1911, xxvi, 522.

⁸⁴ Zeitsch. f. klin. Med., 1907, lxxiii, 420.

⁸⁵ Lancet, 1904, i, 782. Improved methods described in Brit. Med. Jour., 1906, i, 1150; Surg., Gyn., and Obstet., 1908, vi, 29.

⁸⁶ Berl. klin. Woch., 1910, xlvii, 92.

does not state it too strongly when he says that the Cammidge test is "geradezu wertlos." A test which may be positive in health and in a variety of diseases in which the pancreas is normal, and negative when the pancreas is extensively diseased certainly has little to commend it. This opinion is supported by the fact that in 2 dogs in which we produced progressive chronic inflammation of the pancreas by obstructing the ducts the Cammidge reaction was negative.

LOEWI'S TEST. After extirpation of the pancreas in dogs and cats, Loewi⁸⁷ produced dilatation of the pupil by the instillation of adrenalin. He attributes the dilatation to an increased excitability of the sympathetic nervous system. In man he found the reaction in a case of occlusion of the pancreatic ducts without glycosuria. He also obtained a similar mydriasis in 10 out of 18 diabetics, and Falta,⁸⁸ in 15 out of 36 cases of diabetes. Cords⁸⁹ examined 11 cases of diabetes and only 3 were positive. Bittorf⁹⁰ observed the reaction only twice among diabetics, and both of his patients were moribund at the time. In 3 dogs with extreme atrophy of the pancreas I found the test negative, and also in the case of a man who developed diabetes several years after an attack of hemorrhagic pancreatitis.

DIAGNOSIS OF ACUTE DISEASE OF THE PANCREAS. Until recently the functional tests have furnished little, if any, aid in the recognition of acute pancreatitis. I know of no case in which a serious interference with the absorption of fat and nitrogen has been shown. Stockton⁹¹ has recently called attention to the slight disturbance of the fat digestion. I made an analysis in one case and found only 17.4 per cent. of fat in the dried stool; 50.3 per cent. was in the form of neutral fat, 21.6 per cent. as fatty acid, and 28.7 per cent. as soap. There was 5.8 per cent. of nitrogen.

Recent observations on the occurrence of large amounts of diastase in the urine in acute pancreatitis give foundation for the hope that a determination of the diastase in the urine may prove of great aid in the diagnosis.

DIAGNOSIS OF CHRONIC DISEASE OF THE PANCREAS. Pancreatic insufficiency, even of mild degree, can be recognized by the functional methods of diagnosis now available. At the present time no single sign or symptom can be accepted as pathognomonic of pancreatic disease, but by the use of a number of different tests the diagnosis can be made.

The functional tests have already thrown much light on the pathological physiology of the pancreas. Observations made with these tests indicate that diminished or altered secretion of the pancreas may occur without demonstrable anatomical changes in the organ.

⁸⁷ Arch. f. exper. Path. u. Pharm., 1909, lix, 83.

⁸⁸ Wien. klin. Woch., 1907, xx, 1559.

⁸⁹ Die Adrenalin Mydriasis und ihre diagnostische Bedeutung, Wiesbaden, 1911, p. 45.

⁹⁰ Zentralb. f. inn. Med., 1909, xxx, 33.

⁹¹ Trans. Assoc. Amer. Phys., 1911, xxvi, 545.

Within the last few years much interest has been aroused in the diagnosis and surgical treatment of chronic pancreatitis. This has been chiefly due to the papers of Robson,⁹² in England, and those of Deaver⁹³ and William Mayo⁹⁴ in this country.

Riedel,⁹⁵ as early as 1896, stated that in 3 out of a series of 122 cases of cholelithiasis the head of the pancreas was enlarged and very hard.

Many cases have been reported by surgeons during the last twelve years in which the diagnosis of chronic pancreatitis was made. Mayo Robson regards the condition as a clinical entity. He and his followers claim that obstruction of the common duct is frequently due to the pressure exerted by the swollen head of the pancreas.

Opie,⁹⁶ however, in his text-book refers to only 1 case in which occlusion of the common duct by the pancreas was demonstrated at autopsy. Our experiments on dogs show that extreme chronic pancreatitis and atrophy do not interfere with the health of the animal, provided a small amount of secreting tissue remains.

Among the cases reported by surgeons of the type of chronic pancreatitis described by Mayo Robson, I have found none in which the evidence was convincing that pancreatic insufficiency was present, or that the obstructive jaundice was due to pressure exerted by a swollen pancreas. In many cases the symptoms might equally well be attributed to chronic cholangitis. As Riedel⁹⁷ pointed out, the icterus associated with stone in the common duct is much more often due to inflammation of the duct than to mechanical obstruction produced by the stone.

It should be borne in mind that a hard pancreas is not necessarily a diseased pancreas. I know of cases in which the diagnosis of chronic pancreatitis was based on the hard feel of the pancreas at operation, and subsequently at autopsy a normal pancreas was found. It is a matter of common knowledge among pathologists that a normal pancreas may have a consistence of almost stony hardness. These facts are brought forward to emphasize the importance of coöperation between the surgeon, the clinical pathologist, and the pathological anatomist. If the cases which the surgeon at the operating table regards as chronic pancreatitis are examined with the aid of the functional methods of diagnosis, pancreatic insufficiency, if it exists, will be detected. Proof will then take the place of conjecture and knowledge of pancreatic disease will advance.

⁹² *Lancet*, 1900, ii, 236; 1904, 861; Robson and Moynihan, *Diseases of the Pancreas*, Philadelphia, 1902, p. 147; Robson and Cammidge, *The Pancreas: Its Surgery and Pathology*, Philadelphia, 1907, p. 412.

⁹³ *AMER. JOUR. MED. SCI.*, 1903, cxxv, 187; *Jour. Amer. Med. Assoc.*, 1911, lviii, 11; *Amer. Med.*, 1904, vii, 465.

⁹⁴ *Jour. Amer. Med. Assoc.*, 1908, l, 1161.

⁹⁵ *Berl. klin. Woch.*, 1896, xxxiii, 2.

⁹⁶ *Disease of the Pancreas*, Philadelphia, second edition, 1910, p. 244.

⁹⁷ *Loc. cit.*

PELLAGRA IN ITS RELATION TO NEUROLOGY AND PSYCHIATRY.¹

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FOUR years ago there were probably not half a dozen physicians in America who had given pellagra any serious thought, but today it attracts the attention, or should, of every American physician and is of especial interest to the internist, the hygienist, the dermatologist, the neurologist, and the alienist. Previous to 1907 only a few sporadic cases had been observed in this country when Searcy,² of Alabama, during this year, reported 88 cases observed in the State Insane Asylum. Last year there were estimated to be 5000 pellagrins in the United States,³ while this year it is said there are 10,000, some alarmists putting the figure even much higher. The onset of many cases was undoubtedly some years previous to 1907, but the disease was not a known factor in this country until that year. Neither is the disease, as many suppose, confined to the Southern States. Over 200 cases have been reported from the State Insane Asylum at Peoria, Illinois, and I understand that a dozen cases have been diagnosticated at the Philadelphia General Hospital. There are probably but few large charity institutions in the United States in which there is not a case. The question as to how the disease spreads is a large one and has not been settled. It is not considered contagious.

The disease has been studied in this country mainly in institutions for the insane where some of the cases developed, but where most were admitted with pellagra in an advanced stage. The writer⁴ published about a year ago the study of 55 non-institutional cases, and his work since has been chiefly confined to this class of cases. In the present paper, after a brief general description of the disease, it is proposed to take up the study of pellagra from a neurological and a psychiatric viewpoint, to call attention to various symptoms under these headings in the analysis of 88 cases and to make some deductions therefrom.

GASTRO-INTESTINAL AND CUTANEOUS SYMPTOMS. The symptoms of pellagra should be described under four headings representing more or less four different symptom-complexes. First are the gastro-intestinal or alimentary symptoms. The extent of the alimentary canal from the lips to the anus is often inflamed and during the attack some portion will be affected, even if only mani-

¹ Read before the Section on General Medicine of the College of Physicians of Philadelphia, December 19, 1911.

² Jour. Amer. Med. Assoc., July 6, 1907, p. 37.

³ Amer. Jour. Insanity, January, 1911.

⁴ Jour. Amer. Med. Assoc., January 28, 1911, p. 246.

fested by sore mouth. Stomatitis, nausea, vomiting, diarrhea and proctitis are common symptoms of the disease. Most writers have placed the cutaneous symptoms as the first manifestation of pellagra, but a careful review of early cases made by me brought out the fact that at least 80 per cent. gave a history of diarrhea or nausea and vomiting before cutaneous symptoms were noted. I believe if more accurate observations could be made and stomatitis included this percentage would be greatly increased.

The characteristics of the cutaneous lesions are that they are symmetrical, that the backs of the hands are always involved, usually at the beginning, that the lesions extend up the forearm on the extensor surfaces and have a tendency to become annular at the wrists and elbows. Lesions may also appear on the fore-

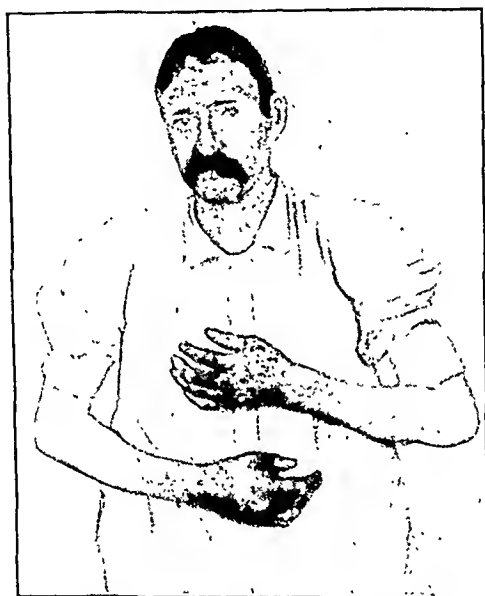


FIG. 1.—Cutaneous lesions of pellagra, showing symmetrical involvement of the backs of the hands and forehead.

head, cheeks, alæ nasi, chin, neck and dorsum of the feet. In the beginning they are usually erythematous in appearance, the skin quickly becoming rough and dark, often fissuring and sometimes sloughing. Bullæ filled with serum sometimes appear. Itching or burning may or may not accompany the skin lesions. As the lesions heal marked desquamation takes place. Accompanying the gastro-intestinal symptoms or the skin lesions, or following them shortly, are nervous manifestations and frequently mental symptoms. These will be taken up separately in this paper as we proceed. Among the general symptoms are loss of weight, moderate secondary anemia, malaise, and weakness. Females are more frequently affected than males and no age is exempt.

COURSE. Pellagra usually makes its appearance in the spring or summer. If the patient lives through the first attack there is a remission during the winter and a return of the symptoms the following spring or summer. Thus there is an acute or fulminating form in which the patient dies in from a few weeks to a few months and a chronic or recurrent form which may last a few or many years. The mortality during the first two years of the disease is over 50 per cent., recurring cases have been known to live fifteen or twenty years. In a few cases, hardly 10 per cent., recurrence does not appear and the patients are apparently cured.

LABORATORY FINDINGS. Neither stomach, fecal, blood or urinary examinations have thrown much light upon the study of pellagra. Absent hydrochloric acid in the gastric juice is reported in many cases, but this is by no means constant. Ameba are frequently found in the stools but have no causative relation. A moderate and sometimes a severe secondary anemia is present. Wassermann reactions are negative. No especial study of the cerebrospinal fluid has been made. This should be done, as it may possibly throw some light upon the subject.

ETIOLOGY. The Italian school has generally accepted the theory that pellagra is caused by a toxin from spoiled maize. This theory has been largely discarded by American students of the disease and to my mind is disproved. Suffice it to say here that pellagra has occurred in localities where corn products were rarely eaten and in persons who stated that they never ate cornmeal bread. Cotton-seed oil, various bacteria, protozoa and fungi have been exploited as the cause, but none of these have been substantiated. Bass⁵ recently stated that he has obtained, chiefly from the stools of pellagrins, cultures of bacteria which, when mixed with meal and water, and fed to chickens, gave a skin lesion said to resemble pellagra. We should certainly not accept this report until absolutely proved on the human subject. Sambon has endeavored to prove that pellagra is due to some product inoculated by the sand fly and lays stress upon its occurrence near streams. Two of my recent cases were in women, neither of whom lived within half a mile of a stream or creek, and both of whom had violent cases, although they practically never went near the stream, while those of the family whose occupation as farmers took them to the stream did not develop it. Beall⁶ has made the same observation in a number of cases occurring in Texas.

The sun rays make the skin lesions worse, but seem to have no other relation, as lesions sometimes develop on the feet of those who wear shoes and stockings, and the lesions in those whose right hands are more exposed are equally severe on their left hands. Warm weather seems to have some special influence and the

cases are better in the summer when a cool spell occurs. Bad personal hygiene, poor food and frail health undoubtedly add to susceptibility to pellagra.

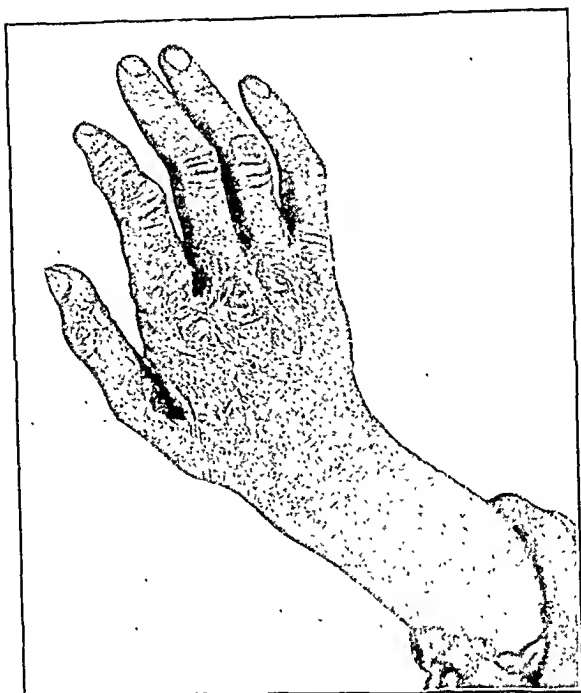


FIG. 2.—Characteristic cutaneous lesion in which the skin has become rough and fissured.

PATHOLOGY. In regard to the pathology of pellagra, we shall have to be brief, and this may be just as well, for we know but little of its pathology. A review of the general pathology shows nothing specific. Harris,⁷ in a study of the pathology of the nervous system, states that there may be noted changes in the chromophilic cells of the cerebral cortex and degeneration of the cells of Purkinje in the cerebellum. Cellular degeneration was noted in various parts of the cord, but no positive evidence of peripheral nerve alteration was found. Spiller,⁸ in a study of the cord in 2 cases, concludes that pellagra does not produce a truly systemic disease of the central nervous system. He thinks the degeneration is caused by some toxic or infectious substance affecting all parts of the cerebrospinal axis, producing cellular degeneration and diffuse degeneration of nerve fibers in the posterior and anterolateral columns.

NERVOUS AND MENTAL SYMPTOMS. We shall now speak especially of the nervous and mental symptoms of pellagra. Your attention is called to the fact that a pellagrin may have nervous

⁷ Trans. National Conference on Pellagra, Columbia, S. C., November 3 and 4, 1909, p. 86.

⁸ AMER. JOUR. MED. SCI., January, 1911.

symptoms without definite mental ones, especially in the early stages of the disease. It is best not to follow the custom of intermingling the nervous and mental symptoms, but to segregate them as much as possible, although they may, and usually do, co-exist. Thus, in the study of these symptoms in 88 cases we find that 100 per cent. showed nervous symptoms and 95 per cent. mental symptoms, the nervous manifestations usually appearing first. Several of the cases had been nervous for years, but their symptoms increased when pellagra developed.

NEUROLOGICAL SYMPTOMS. Among the neurological symptoms we have restlessness in 84 per cent., insomnia in 88 per cent., muscular weakness in 92 per cent. of the 85 cases tested, and muscular wasting was noticed about in proportion to the loss of weight, which was practically constant. Local atrophies or dystrophies were not noticed. Vertigo was present in 76 per cent. of 81 cases. Headache was present in 60 per cent. In regard to sexual power the question was answered in only about one-third of the cases, and it was lost in 25 per cent. of these. Tremors were noted in 53 per cent. of the cases. The tremors chiefly involved the hands and tongue. Cramps were noted in 50 per cent. of the cases and were variously located in the abdomen, legs, arms, thighs and backs. Exophthalmos was noted in 3 per cent. of the cases and seemed to have no special reference to the disease. Of the more organic symptoms, anesthesia of areas of the cutaneous surface was noted in 20 per cent. of 69 cases tested. The mental condition of many of these cases precluded definite interpretation. Tenderness of the spine to percussion was noted in 20 per cent. of 54 cases tested. Contraction of the limbs was noted in 5 per cent. of the cases and was usually transient. Trophic disturbance excluding cutaneous lesions were noted in 13 per cent. of the cases and was chiefly manifested by roughening and thickening of the nails. Paralysis occurred in 7 per cent. of the cases, 3 of these showed paraplegia, 1 hemiplegia, 1 monoplegia and 1 paralysis of the sphincter ani. Rhomberg symptom was present in 57 per cent. of 66 cases tested. Ataxia was frequently present in severe cases but not numerically recorded. Knee-jerks were present in 88 per cent. of 74 cases tested, in 62 per cent. of these they were exaggerated on both sides, in 1 case they were exaggerated only on one side. In 9 of the 74 cases the knee-jerks were absent, in 7 they were decreased. Ankle clonus was not regularly tested, however, I have tested it in many cases which had exaggerated knee-jerks and found it not present. The same may be said of the Babinski phenomenon. The pupils in size were normal in 55 per cent. of the cases, contracted in 20 per cent., and dilated in 25 per cent. In only 2 of these cases were they noted to be unequal in size. The pupils reacted normally to light in 83 per cent. of 79 cases tested. Reaction to light was absent in 6 per cent. and sluggish in 11 per cent. Speech difficulty

occurred in 40 per cent. of the cases. In 2 cases aphasia was noted, in 6 mutism and in the rest speech was described as mumbling, slurring, or weak. Investigation of the special senses showed that smell was affected in 23 per cent. of the cases, in all of which it was diminished. Hearing was affected in 15 per cent., a diminution only being noted. Taste was diminished in about 50 per cent. of the cases, but this test was obscured by the almost constant and often severe stomatitis. Touch changes were noticed when the patients touched objects with their finger balls in 29 per cent. of the cases, being diminished in all except 2 cases in which it was increased. The only sight changes were errors of refraction. Neither diplopia nor photophobia were noticed.

PSYCHIATRICAL SYMPTOMS. A study of the mental condition of these patients showed emotional irritability manifested either by excessive weeping or outbursts of temper in 53 per cent. of the cases. Depression was present in 84 per cent. of the cases and in about half of these the patients were said to have ceased laughing since the onset of the attack. Memory was distinctly poorer than usual in 74 per cent. of the cases. Delusions and hallucinations were present in about 20 per cent. of the cases. Most of the delusions were those of persecution and were unsystematized, and the hallucinations were the usual ones of sight and sound. These symptoms are much more common among institutional cases. Apprehension, varying from anxiety about their condition to delusions of impending danger, was present in 100 per cent. of the cases. Homicide was not attempted in any of these cases, but suicide was committed by 1, attempted by 2, and threatened by 6.

NERVOUS SYNDROME. The nervous syndrome of the pellagrin may then be said to consist of restlessness, insomnia, muscular weakness and vertigo as almost constant symptoms, with headache, tremors, cramps, changes in the knee-jerks and pupil lay reflex, sway in station and slowness of speech occurring in about one-half of the cases, while areas of cutaneous anesthesia, loss of sexual power, tenderness of the spine, and diminution of smell and of finger touch are found in about one-fourth of the cases. Trophic disturbances, contraction of the extremities, ataxia and paralysis sometimes occur. Many mild or early cases only show restlessness, weakness, insomnia and vertigo, while all of the severe cases with which I am familiar show deep reflex, pupil and special sense changes before death.

MENTAL SYNDROME. The mental syndrome of these non-institutional cases shows apprehension, depression, emotional irritability and failing memory as common symptoms, with delusions and hallucinations and suicidal tendencies not infrequent. The mental symptoms, except apprehension, may be absent in mild or chronic cases and severe cases may occasionally go on to

death without developing delusions or hallucinations. All of the severe cases show depression, emotional changes or failure of memory. The severe mental symptoms somewhat resemble melancholia, but they are usually accompanied by neurological signs not found in melancholia, the melancholia depression attitude is not often assumed, the agitation shown by wringing the hands is not seen and delusions of unworthiness are not present. Some of the mental states are said to resemble mania, but I have never seen the flight of ideas, the chaotic delusions, the changes of personality, the exaltation or the increased strength so common in acute mania.

In fact, neither the nervous nor mental syndrome of pellagra corresponds to any known nervous or mental disease, nor, indeed, do they hew closely enough to any one line to form a true clinical entity, but appear to be due to the action of some general toxin or organism. This opinion, as far as mental symptoms are concerned, agrees with that of most of the pellagrologists, who have studied the disease in insane asylums. I have not been able to find a previous attempt to more or less segregate the nervous from the mental symptoms. This attempt was thought justifiable after observing many cases of mild chronic pellagra for several years who did not show any real insane symptoms.

TREATMENT. Only a few words as to treatment will be mentioned in this paper. Urotropin has been used by me or at my suggestion in 20 odd cases and in all cases, with the exception of 2, who lived long enough to take the drug in doses of 10 grains four times a day for ten days either recovered from the attack or, as in 2 other cases, recovered all but their mental symptoms. One typical case has had no symptoms since 1909. A recent report by King and Crowell⁹ seems to show the administration of salvarsan almost a specific. I have not yet tried this. I have certainly not been impressed with any other drug than hexamethylenamine. With the drug treatment as much nourishment as can be assimilated should be given and residence in a far Northern clime may be tried.

CONCLUSION. In conclusion I shall say that although there have been various small sums raised for the study of pellagra, and the next Congress will be asked for an appropriation of \$50,000 for this purpose, and the New York Post-Graduate Laboratories propose to send workers into the field next spring and a small hospital for pellagrins has been opened in Georgia, the magnitude of the problem has not been appreciated. The disease threatens to be a national calamity, for it is both increasing in the Southern States and spreading North and West. No richer field for study may be found for medical investigators and no disease bears the same interest to workers in as many distinct lines as pellagra.

⁹ Jour. Amer. Med. Assoc., November 18, 1911, p. 1687.

Money is needed, not to send small independent commissions into various sections, but to form a large central commission with organized branches all over the field. The problem will, of course, eventually be solved, but we are primarily a life saving profession, and every summer which is allowed to go by before it is solved means the death of many thousands of our citizens.

GASTRIC OR INTESTINAL HEMORRHAGE AS AN EARLY MANIFESTATION OF A GENERAL TOXEMIA.

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GASTRIC or intestinal hemorrhage has been frequently observed to occur in the course of various pathological conditions. It is not the purpose of this paper to discuss the hemorrhages occurring with such infectious diseases as measles, scarlet fever, or variola, but those of purely septic or toxic origin. Dr. W. J. Mayo,¹ in a paper presented at the last meeting of the American Surgical Association makes the following statement: "Toxic erosion of the gastric mucosa is the usual cause of the gastric hemorrhages which accompany cirrhosis of the liver, splenic anemia, and certain disordered blood states." Henschen² refers to the occurrence of these erosions in tuberculosis, nephritis, brain disease and pneumonia, and says that the fact of their occurrence justifies the inquiry whether they are not dependent upon general instead of local conditions.

The writers of this paper will not enter deeply into a study of the etiology, but in presenting a few cases for your consideration, prefer to have this contribution considered as suggestive rather than conclusive.

Whether profuse gastric hemorrhage can occur without gross pathological lesion is a subject to which English surgeons and pathologists have in recent years given their attention. The term gastrotaxis has been applied to a condition in which free oozing of blood from the mucous membrane of the stomach occurs, and in which there is no evidence of ulceration of that organ nor other pathological process from which bleeding is likely to occur. Bolton,³

¹ Annals of Surgery, September, 1911, p. 313.

² Wied. medicin. Presse, 1902, No. 46.

³ Brit. Med. Jour., May 21, 1910.

in discussing this condition states: "In severe anemias, in infective disease, in purpuric conditions, in toxemias associated with disease of the liver and kidneys it is a common experience to find the mucous membrane of the stomach intact when vomiting of blood has occurred during life." It is to the class of cases in which hemorrhage from the stomach or intestines occurs as the initial symptom, without pathological disorganization of the mucosa or the presence of an ulcerative process of any kind that we wish to call attention.

Singularly enough hemorrhage has occurred in the newborn much more frequently than in the adult. Our literature presents a great array of observations on this class of cases. It has been suggested that in many instances syphilis is responsible for this hemorrhagic condition in the newborn. That it is by no means a constant factor is generally admitted. Serious hemorrhages can occur, with perhaps no explanation for their occurrence. The following is an illustrative case.

E. S. was born October 27, 1905. Both of her parents are vigorous and free from any syphilitic taint. Dr. A. G. Doust delivered the child without instruments, and the labor was in every way perfectly normal. The child was apparently well until she was three days old. On that day she had two very profuse gastric hemorrhages, and one of us (Dr. Jacobson) was asked to see her with the attending physician. On the following day there were several discharges of blood by the bowels. In some of the bowel movements the blood appeared black, and in others it was of brighter color and profuse enough not only to saturate the napkins, but the bedding as well. Adrenalin was administered. The hemorrhage ceased after the fourth day, and the child recovered. In the six years which have elapsed she has had no sickness, and particularly no evidence of gastric or intestinal derangement. There are two other children in the family, both of whom are well, and there is no hemophilic tendency in any branch of the family. It would be difficult to assign a cause for the hemorrhage in this case. The child had no fever nor other evidence of a toxic condition. The fact that she so promptly recovered and has remained well since would seem to be conclusive that no serious pathological process existed at that time, and that the condition was probably dependent upon some temporary disturbance, which after all might have been toxic.

Our second case one of us (Dr. Jacobson) saw in consultation with Dr. McLennan at the Syracuse Hospital for Women and Children on May 26, 1905. This child was then two days old. She had been delivered after a protracted labor which lasted into the third day, by Dr. Sears, who was finally obliged to apply the forceps. The mother had not been well for some days, and Dr. Sears informed me that the amniotic fluid was exceedingly foul.

Three hours after birth the child had a temperature of 99.6° . On the following day her temperature was 100.5° in the morning and 104.4° in the evening. During the first twenty-four hours she vomited a dark brown substance. On the second day, material of the same character was repeatedly vomited. When the patient was thirty hours old, blood and mucus were found in the stools. When I saw the child, she was still vomiting blood and likewise passing blood with the stools. She had had a general convulsion. The skin was not jaundiced, nor were there any petechiæ on the body. Her temperature had been 104.2° at nine in the morning, and at the time of my visit was 102.2° . On the next day the bleeding from the bowels was less pronounced, and the child had a bloody discharge from the vagina. Its intestinal tract had been cleared out with calomel followed by citrate of magnesia, and the large intestine washed out with a normal saline solution. The mother was advised not to nurse the child. By May 29 there was no more blood to be discovered either in the stools or from the vagina. On June 2 the child was again put to its mother's breast on three occasions, and each time it suffered a great deal of distress and vomited sour curdled milk. No further attempt was made to have the mother nurse the child, and from this time forward, with careful regulation of artificial feeding, no further unpleasant manifestations were experienced.

Hemorrhage of the newborn of toxic origin, and in this class we must without doubt place this last case, is usually regarded as a very serious condition. Townsend,⁴ of Boston, collected 709 cases in which a mortality of 79 per cent. occurred. That this condition is not of frequent occurrence is evident from the fact that in 5225 births at the Lying-in Hospital in Boston, but 32 instances of this kind are recorded, that is, a little over 0.5 per cent. At the Lying-in Asylum of Prague, in 13,000 births it occurred 190 times, or in about 1.4 per cent. of the newborn. Hemorrhage of the newborn was one of the subjects discussed by the section on diseases of children at the annual meeting of the American Medical Association in 1906. Litzenberg,⁵ in that discussion, referred to the case of a babe who thirty-six hours after birth had hemorrhages from the mouth and intestines, the loss of blood being so great that it resulted in death when the child was fifty hours old. At the autopsy innumerable submucous hemorrhages were discovered beginning at the cardiac orifice of the stomach and extending to the rectum, increasing gradually in size from above downward. From these hemorrhagic areas a pure culture of the bacillus of Friedländer was recovered.

One of the most excellent papers on the subject of hemorrhage

⁴ Quoted by McClannahan, *Jour. Amer. Med. Assoc.*, October 13, 1906.

⁵ *Jour. Amer. Med. Assoc.*, October 13, 1906.

of the newborn due to septic or toxic conditions was presented by von Dungen.⁶ The literature on this subject is very carefully reviewed by him, beginning with the work of Weber in 1854. Klebs, in 1875, was the first to discover microorganisms in the hemorrhagic areas. He succeeded in producing hemorrhagic peritonitis in a rabbit by inoculating it with the hemorrhagic peritoneal fluid taken from a child who had died of this condition.

Rehn, in 1877, reported the case of a child who died three days after birth from hematemesis and bloody evacuations from the bowels. At autopsy some thirty points varying in size from a pin-point to a pin-head were found in the mucosa of the stomach. Each presented an infiltrated base, in which microorganisms were found. Babes, of Bucharest, was one of the earliest contributors to this field. He discovered specific organisms not only in the hemorrhagic areas, but also in infarcts in the spleen and lungs of a child dying when aged five days, and these he stated resembled the capsulated cocci of pneumonia. V. Dungen concluded that these hemorrhages resulted either from emboli or the damage done to the vessel walls by the production of toxins. In the inoculation of animals the pathological changes he stated are found to be due to the latter. He is rather inclined to believe that the hemorrhagic conditions of early life result from the toxins rather than the bacillary invasion.

Let us consider next the occurrence of gastric or intestinal hemorrhage as the initial manifestation of a toxemia in the adult. Permit us to present 2 cases. In one the hemorrhage was not externally visible, while in the other it was exceedingly profuse.

The first case has been fully reported in the *Medical Record* of February 7, 1903, and, therefore, at this time will only be summarized. It concerned a woman, aged thirty-seven years, who was suddenly seized with acute abdominal pain, at first general, and finally becoming centered in the right side of the abdomen. The only difference between her suffering and that encountered in the ordinary cases of appendicitis was that while the most acute point of pain and tenderness was at the characteristic site of the appendix, there was also severe pain in the region of the gall-bladder and umbilicus. There was marked resistance of the right rectus muscle, which was not altogether limited to the lower half. The temperature was 104.5°, and the pulse rate, 132. One of us (Dr. Jacobson) operated upon her on February 23, 1910. Bleeding was exceedingly profuse. The appendix was found to be 5 inches long, apparently acutely inflamed, at least it was exceedingly red. It contained a mucoid secretion which was not bloody, but in the substance of the appendix there was marked interstitial hemorrhage, which was responsible for the decided enlargement of the

⁶ Zentralbl. f. Bakter. u. Parasitenkunde, October 28, 1893.

organ. Nothing unusual occurred in the progress of the case until the fourth day, when the patient developed a hacking cough, and raised a large quantity of bright red blood. During the same night she had a profuse nasal hemorrhage. On the following day petechiæ appeared on the surface of the body, first on the left leg near the head of the fibula, and then numerous ecchymoses showed themselves on the calves of both legs. On the abdomen numerous petechial points were likewise found. The heart at no time presented a murmur nor any other evidence of disease. The joints were not implicated. She never had visible hemorrhage from the intestines or stomach, nor was there hematuria. Nasal hemorrhages were very profuse and frequent, and the bronchial hemorrhage most persistent. The latter continued for nearly three weeks. Whenever she was given a hypodermic injection she bled freely from the puncture of the skin. She made a slow recovery, and has never had any hemorrhagic disturbance since. No member of her family has been a hemophilic. The case was reported as one of purpura, in which the earliest manifestation was hemorrhage into the substance of the appendix.

In reviewing the literature at that time I called attention to a paper published by Professor Henoch.⁷ He referred to 4 cases which had come under his observation, all of them occurring in early life. The ages of his patients were four, eleven, twelve and fifteen years respectively. Three of the patients suffered from characteristic joint disturbances which appeared in advance of any gastric or intestinal symptoms. Each of the 4 suffered from pronounced intestinal hemorrhages, but none of them from hemorrhage of any other mucous surface. In each of these cases there were periods of remission and recurrence so that one patient had five attacks in the course of seven weeks, another four in as many weeks, the third had five recurrences and the fourth a similar history. In none, however, was there any evidence of disturbance in the region of the appendix. Each of his patients suffered from marked abdominal tenderness and vomiting, as well as intestinal hemorrhage. The intestinal pain was so severe as to cause loud outcries on the part of his patients, to rob them of sleep, and was associated with marked distention of the abdomen as well as tenesmus. The temperature in all of them was moderate. Each made a good recovery. As, however, his cases were reported in 1874, before the days of bacteriological study, there was no determination of their etiology.

Our last case is of a quite different type. The following history is furnished by one of us (Dr. Post).

M. H., married; aged forty-eight years, inspector of coal, was seen April 8, 1911. He complained of being exceedingly weak and

⁷ Berl. klin. Woch., December 21, 1874.

faint. His family and personal history were free from tuberculosis, malignancy, rheumatism, and syphilis. He stated that he had always been well until ten days before. At that time he complained of pain in the lower part of the left side of his chest, which was aggravated by coughing. He consulted his family physician at Newark, N. J., who strapped the chest. The patient in the meantime having been sent to this city to inspect some coal, continued to work until the present illness. On April 6, 1911, in the evening, while at dinner, he became faint. He finished his meal, however, and indeed worked on the following day, but noticed that when he would get up from a squatting position he became dizzy. On April 7 he was about the hotel. He had no desire for food, and during the morning had three or four black tarry stools. That night he was restless, and did not sleep well. When seen on April 8, 1911, he was confined to his bed, was pale, but complained of nothing but weakness. He was anxious to return to his home in Newark, but evidently was not well enough to make a railroad journey of more than three hundred miles. The pallor of his conjunctivæ, lips and mucous membranes suggested that he had sustained a considerable loss of blood. The pulse was 100; temperature normal. Physical examination of the chest was negative. On the left side of his chest and back there were the marks of the adhesive plaster which had been removed. On this date the heart was found to be of normal size. The sounds were faint, but there were no murmurs. The liver and spleen were of normal size. There was no abdominal distention nor tenderness. Rectal examination was negative. April 9 his condition became alarming. The pulse rate was 120; its quality was small and very weak. During the night he had vomited once, the vomitus containing a quantity of fresh blood. The heart sounds had somewhat changed. There was a soft systolic murmur to be heard at the left sternal margin opposite the fourth rib. He was transferred to St. Joseph's Hospital and was there seen in conjunction with Drs. Flaherty and Jacobson. The respirations on admission were 24, pulse, 128; but so weak that it was hardly perceptible. The temperature on admission in the morning was 100.4° per rectum, and at two o'clock in the afternoon it rose to 101.4°, at six o'clock had fallen to 101°, and at ten o'clock to 99.8°. On admission into the hospital he complained of pain in the epigastric region but this disappeared after he was catheterized. He had no abdominal pain nor distress except when the bladder became distended. Each time that he was catheterized at least twenty ounces of urine were withdrawn. On being questioned, he, as well as his wife, stated that he had never had any previous gastric or intestinal disturbance, and that at no time in his life had he suffered from indigestion, abdominal pain, nor anything to suggest a pathological condition in the stomach or abdomen. Physical examination of the abdomen did not reveal

at the time one of us saw him in consultation, any tenderness, rigidity, or dulness. The heart murmur steadily increased, and could be heard loudest on a level with the nipple at the left sternal border. It was least distinct at the base, and was associated with the first sound. On the left side of the chest and corresponding with the area to which the adhesive straps had previously been applied were a number of pigmented spots, which did not fade out on pressure. A blood count was made, and it was found that the hemoglobin was 55 per cent.; red blood cells, 2,250,000; white blood count, 7,000. Dr. F. M. Meader was requested to make a blood culture. His report read: "Specimen consists of about 7 c.c. of blood put into two flasks, each containing about 150 c.c. bouillon. Diagnosis: Pure culture of pneumococcus." His bacteriological diagnosis was based upon the morphological features alone. He made no further cultures upon other media, nor did he make any inoculations. Had he done so, he stated that possibly he might have decided that we were dealing with a capsulated bacillus of the Friedländer group, but not necessarily the pneumococcus.

The patient required catheterization for the first five days after admission into the hospital. The bowel movements continued to be black for four days, evidently containing large quantities of blood. Urinary analysis never revealed any abnormal condition. Blood examinations showed steady improvement. On April 16, the hemoglobin had increased to 60 per cent., the red blood cells to 3,000,000, and the white blood cells numbered 7800. On April 22 the hemoglobin percentage was 65, red blood cells, 3,170,000; and white cells, 5600. At this time he was able to take ordinary foods; had gained in strength, and was able to sit up. The heart murmur had entirely disappeared, and there had been no further evidence of hemorrhage in any form. The temperature continued slightly elevated for a few days. He was discharged from the hospital well on May 8, 1911, and has continued to enjoy excellent health since.

It is evident that in this particular case a capsulated bacillus, probably the pneumococcus, was responsible for the toxemia which produced such a profuse hemorrhage from the intestinal tract. Evidently the site of the disturbance was the duodenum, inasmuch as it was associated with marked gastric hemorrhage. It seems fair to assume in view of the chest manifestations which preceded the intestinal disturbance, that the portal of entry of the infectious organism was pulmonary.

The literature of this class of cases is not abundant. That capsulated bacilli are responsible for gastric or intestinal hemorrhages has been thoroughly established by Howard.⁸ After carefully

⁸ Jour. Exper. Med., March, 1899.

reviewing the literature and work of others, and as a result of his own studies, he concludes that in the cases of hemorrhagic septicemia there has been found each time a pleomorphic capsulated bacillus. Speaking of the manner in which these capsulated bacilli differ, he says: "Of these differences the chief relate to the various amounts of gas and acid production, the capability and rapidity of the coagulation of milk, the behavior of Gram's stain, and the widely varying results of animal inoculation." He reaches the conclusion that various bacteria, not only those of the group mentioned, but streptococci and others as well, may cause hemorrhagic infection of human beings. Hemorrhagic septicemia is, therefore, not to be regarded as a separate and distinct disease with definite and constant etiology, uniform anatomical lesions and clinical features, but rather as a toxemia attended by such marked injury to the bloodvessels and to the blood as to cause extreme dilatation of the vessels and hemorrhages with various harmful effects upon the body cells. Some of the cases have manifested a rapidly malignant course, while others have been of a milder type and of longer duration.

That the pneumococcus is capable of producing such a hemorrhagic condition has been clearly demonstrated by Claisse.⁹ He refers to an unpublished case in the service of Hutinel at the Hopital des Enfants, in which purpura followed upon pneumonia, and in which the pneumococcus was recovered not only in the purpuric areas of the skin, but also in infarcts in the kidneys and spleen, as well as from the endocardium. The character of the microörganism was further established by the inoculation of mice and by cultures. He also demonstrated that the pneumococcus can enter the body and produce widespread pathological changes before it awakens a pneumonia.

In this case reported in detail by Claisse he was unable to determine the portal of entry of the pneumococcus. At the time of the admission of the patient into the hospital he was covered with purpuric spots, and was suffering from endocarditis and nephritis. The patient, a young man, aged twenty-two years, had been in good health until, while rendering military service, he had an attack of rheumatism. This became complicated with endocarditis, and thereafter he suffered from dyspnea on the slightest exertion. He had also marked periods of palpitation of the heart, and frequent attacks of bronchitis accompanied by mild hemoptysis. He was poorly nourished, and had become reduced in strength. When admitted into the hospital the petechiæ covered both of his lower extremities, the distribution being symmetrical. There was an increase of splenic dulness and the spleen was large and tender. The precordial region was painful, and there was

⁹ Archiv. de med. experimentale et d'anatomie pathologique, 1891, iii, 379.

increased precordial dulness. A mild systolic murmur could be heard radiating toward the armpit. Examination of the lungs was negative. The urine contained a large percentage of albumin. Two days later he was seized with severe pain in the right side of his chest, associated with a prolonged chill. Respirations became labored and frequent. He coughed a little, and expectorated bloody sputum. Then appeared the usual physical signs of pneumonia, involving the base of the right lung, and from this he did not rally. The autopsy justified the conclusion that while the man had had an old endocarditis resulting from the attack of rheumatism, he had in some way become infected with the pneumococcus, and an acute pneumococcic endocarditis resulted. None of the organisms were found in the older lesions of the endocardium. Pneumococci were recovered from the spleen and from the kidneys, as well as from various purpuric macules of the skin. Cultures were made on agar and gelatin, and in bouillon. Animals were also inoculated. In these different ways positive proof of the pneumococcic origin of this case was established.

V. Babes¹⁰ has likewise carefully investigated the subject of the bacteria responsible for hemorrhagic infections in the human being. He also attempted to determine whether a single microorganism is responsible for all types of hemorrhagic infections. He concludes that no single specific organism is responsible therefor. He analyzed in his article the labors of other observers as well as his own, and arranges in columns, for the purpose of comparison, the clinical and laboratory features of the various microorganisms. He studied their behavior upon various culture media, and by the inoculation of animals. He was able to determine that bacteria which cause hemorrhagic septicemia in animals do not conform in all respects with those which produce this disturbance in man. He concludes, however, that all of these bacteria possess the common property of having a specific effect upon the bloodvessels causing molecular destruction either of the vessel walls or hyalin degeneration of the bloodvessels. Some of the results he also concludes are due to changes in the blood, and that the toxic products of bacteria are capable of producing not only the purpuric conditions, but can also cause excessive hemorrhages.

Spencer¹¹ states that the peculiarity of septicemic or toxic hemorrhage from mucous or serous surfaces is their occurrence without the production of a naked eye breach of the surface.

From the foregoing it is evident that certain microorganisms, particularly those possessing the characteristics of the pneumococcus are capable of provoking severe hemorrhages in various parts of the body, and that gastric and intestinal hemorrhage can be the first evidence of such a toxemia.

¹⁰ Zentralbl. f. Bacter. u. Parasitenkunde, 1891, ix, 719.

¹¹ Brit. Med. Jour., December 24, 1910.

THE DIETETIC AND GENERAL MANAGEMENT OF TYPHOID FEVER IN CHILDREN.¹

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IN the selection of food for children in health we are governed by certain well-recognized principles. For proper growth and right development both physical and mental, the food given must be of adequate nutritional value. This constitutes the science of feeding. It must be prepared so that it may be assimilated by the organism. There must be a variety in form and it must be attractive to the senses of taste and smell, and this is the art of feeding.

In illness we have the same child to deal with and the same factors are in control and must be respected even in greater degree than in health, for then we have not that margin for error which health permits. The child ill requires food of a definite nutritional value in assimilable form. This is the science of feeding in sick children. It requires variety and it is necessary that the food selected be made agreeable to the patient, and this is the art of feeding in sick children.

There is no ready-made diet in any illness in a child, neither is there one ready-made scheme for the artificial feeding of infants ill with digestive derangements. Feeding, then, both in sickness and in health, is an art as well as a science, and in the feeding of sick children the art is of equal importance with science. I find it necessary at the onset of every illness to discontinue milk and so-called solid foods, for the reason that in every illness in a child the capacity for food is lessened, and to what degree it is lessened I make it my business to find out. I give a laxative sufficient to produce a few watery evacuations. As a temporary diet, the child is given flavored gruels and perhaps one of the dried milk foods, until the nature of the illness is determined. In typhoid fever the diagnosis is rarely made under a week of observation.

Following out the above management, when the diagnosis is established, we have an intestine free from distention with gas and undigested milk, and we have consequently a patient less toxic and with a lower temperature than would have been the case had freer feedings been allowed. With the diagnosis of typhoid fever positive, I dictate a list of permissible food articles. We will assume that the patient is five years of age. The diet schedule includes gruels, usually two ounces of the cereal to the pint of

¹ Read before the Section on Diseases of Children at the New York Academy of Medicine, November 9, 1911.

water. Gruels are made palatable and their nutritional value increased by the addition of broths or milk sugar or sherry wine. Cereals very thoroughly cooked such as rice, farina, and cream of wheat are served with butter and cane or malt sugar or with maple syrup and butter. Milk foods are rarely given oftener than once a day. Among those used are matzoom, kumyss, Eiweiss Mileh of Finkelstein, and skimmed milk. The latter is always given mixed with a gruel and rarely oftener than once a day. The whites of two, three, or four eggs are given daily with orange juice, or frozen with orange juice and cane sugar and served in the form of a sherbet. Lemonade and weak tea, both with the addition of cane sugar, are given between the regular feedings. Early in the convalescence scraped rare steak, custard, soft boiled egg, and junket are allowed. It is advisable to feed the patient lightly for the first few days, until the organism adjusts itself and adapts itself to its changed condition, when freer feeding may be allowed.

It is entirely wrong to assume that the diet we begin with must be continued throughout the attack. Food will be tolerated during the latter part of an illness which could not be taken during the earlier stages. Feedings are given never oftener than at three-hour intervals or less than four hours, in quantities that we know from observation the child will be able to take care of. One of the reasons for the considerable variety is that children soon "go stale" on any one article of diet; if given persistently, it is refused or taken in small quantities. If it is forced, it is very apt to be vomited; or if retained, the child in all probability will not digest it.

The diet schedule for our typhoid patient, aged five years, would be something as follows:

6 A.M. Eight ounces of gruel with sugar or a small amount of broth added. Zwiebaek or dried bread and butter.

8 A.M. A drink of weak tea with sugar or the whites of one or two eggs with sugar in orange juice.

10 A.M. Farina, cream of wheat, rice, served with butter and sugar, or maple syrup and butter. Drink of weak tea or kumyss or matzoom, or perhaps a dried milk food, such as malted milk or Nestle's Food.

2 P.M. Eight ounces kumyss, matzoom, or skimmed milk diluted with gruel. Zwiebaek; dried bread and butter if wanted.

4 P.M. Orange egg sherbet or a drink of lemonade or tea and sugar.

6 P.M. Cereal or gruel with sugar and butter or with broth. If skimmed milk has not been given at two o'clock it may be given with gruel at this time.

10 P.M. Gruel with sugar or broth or with wine.

It will be seen that the caloric requirements, 60 to 70 per kilo for the five-year-old child, may easily be supplied by the above

arrangements of the feeding, although the diet arranged may not be an ideally balanced one. It would be high in carbohydrates, rather low in fat, and perhaps deficient in protein, particularly during the earlier period of the treatment.

Fat in considerable quantity is poorly digested by young typhoid fever patients. It may be given, however, in small amounts when mixed with other foods. Foods containing protein should not be given in considerable amount until we know something of the course of the disease. Milk, scraped beef, and soft boiled eggs are not well borne in young typhoid patients and a temporary reduction of protein is not felt by them.

Carbohydrates such as the cereals and the different sugars are readily cared for when properly prepared and administered. They supply fuel and no bi-products and do not require immediate elimination from the body. Emaciation is prevented through their action as proteid spacers. Mendel and Rose, in the *Journal of Biological Chemistry*, state they found that the excretion of creatin, induced by starvation, is inhibited in rabbits by feeding a diet of carbohydrates, absolutely free from proteins and fats. When the carbohydrates are given in liberal amounts the creatin entirely disappears from the urine. The creatin eliminated is not reduced by feeding a diet of fat alone or by a diet of fat and protein. Experimental interference with carbohydrate metabolism leads to the elimination of creatin, the presence of the creatin being due to a true tissue or endogenous metabolism.

Why not a milk diet? I have used the milk diet and have seen it used in many cases. Because of an early selection of a medical career, I came in close association with country physicians. It is on the farm and in the country village, where the well and the vault for the sake of convenience are built as close to the dwelling as possible, that we find typhoid fever a frequent visitor. I have watched many of these cases ill with typhoid fed on text-book milk, and I have seen the distended abdomen, the high, protracted temperature, the prolonged and active delirium, and later I filled out the certificate, all but the signature. These patients were given milk in copious amounts at two- and three-hour intervals, and milk constituted the sole food and drink. The milk diet is popular because many physicians have never tried any other means of feeding and it is the easiest way. It is easy for everybody but the patient, and he is not consulted. It is easy for the physician, it is easy for the nurse, it is easy for the household; it is much easier for the doctor to order so many pints of milk a day than it is to write out a diet schedule of right caloric values and explain the preparation of the foods suggested.

The mixed feeding is not employed, further, for the reason that physicians fail to realize that other foods may be taken care of easier than milk, and because of the fear of lay criticism for depart-

ing from an established practice. That many people have recovered from typhoid on the milk diet is not to be questioned. That many have not recovered is equally true. We know that typhoid fever is a disease of small mortality. In spite of former unfavorable impressions as to the milk diet in typhoid I used it early in my medical practice because I had been taught that it was right, and if the patient did not do well it was the fault of the patient, and that the system was the correct one. Another very good reason for using milk was that I have never been taught how to use anything else.

My favorable experience in intestinal diseases with a diet other than milk, together with the teaching of Dr. A. Seiber, of New York, led me to use somewhat similar means of feeding typhoid fever patients.

Mortality statistics do not teach us all that may be learned regarding the disease or a method of treatment. The time element as relates to the duration of the illness and the duration of the convalescence is important. My observation in the milk-fed cases is that the illness is more severe, increasing the danger to life, and that the duration of the illness is longer. Emaciation is much greater and the convalescence is consequently much more protracted than those fed as I have indicated. The case in which the temperature period is cut down to from fourteen to twenty days, with little emaciation and prompt convalescence, should not be put in the same class with the case in which the fever lasts from thirty to fifty days or longer, with a convalescence of three or four months, although both had typhoid fever and both recovered.

It is argued that milk is the ideal diet, and the reason given is that it contains all the nutritional elements required by the organism—fat, protoid, carbohydrate, and mineral salts—which is the truth. It is further claimed that milk may be taken in large quantities and be readily digested, which is not true in sick children. The addition of pepsin, hydrochloric acid, etc., has been of no value. I have learned that in order to have a short case and a mild case, the abdomen must be kept flat. Tympanites is an indication of danger regardless of how it is produced. On the milk diet, tympanites is the rule. On the mixed diet suggested, it is the exception. So long as I can keep the belly flat, I know I have the case reasonably well in hand.

Drugs have been of no service, except to produce an evacuation when there are not two in twenty-four hours and to control the evacuation when there are more than four in twenty-four hours.

Most children will be perfectly comfortable with a temperature of 104° or slightly over. Under such conditions no attempt at reduction is made. In most cases, restlessness and more or less irritability will appear when it goes higher. In such instances

hydrotherapy in the form of the cool pack is used. The child's thorax and abdomen are wrapped in a towel at 95° and then the towel cooled by sprinkling with colder water.

For the conservation of vitality, the nervous manifestations must be controlled sufficiently so that the child gets adequate sleep. The pack with cold to the head will usually relieve the restlessness, irritability and sleeplessness.

The advantages claimed for the method of management, briefly outlined, is a milder course, shorter duration, more prompt convalescence, and usually, absence of complications.

VACCINATION AGAINST TYPHOID IN THE UNITED STATES ARMY.¹

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THE British Army, on the recommendation of Sir A. E. Wright, then an officer in the British Medical Corps, first used antityphoid vaccination for the purpose of rendering troops immune to typhoid. Major F. F. Russell, of the Medical Corps of the United States Army, after a thorough investigation, made a favorable report to the Surgeon General of the use of this measure of prophylaxis, with its results in both the British and German Armies.

A Board of Medical Officers, consisting of the Surgeon General, Major Russell, and several of our distinguished members of the Medical Reserve Corps, was convened at Washington for the purpose of considering the advisability of its adoption in our Army. As a result, in the early part of 1909, on the recommendation of the Board, the War Department authorized its use in the case of volunteers for inoculation.

On the assembly of Maneuver Division on the Mexican border in the spring of last year, all of the troops, numbering 12,801, were subjected to the typhoid prophylaxis. They remained in camp for four months, from March 10 to July 10. Only 2 cases of typhoid occurred during the entire period of encampment. One case of a very mild type, occurring in a private of the hospital corps, who had not completed his immunization, having taken only two doses. The other case occurred in a civilian teamster who had not been immunized.

¹ Read before the Section on General Medicine of the College of Physicians of Philadelphia, November 27, 1911. Published by permission of the Surgeon General.

Our results during this period are being criticized by some, who say we would not have had typhoid in the absence of the prophylactic inoculations. As our principal camps were located at San Antonio and Galveston, the existence of typhoid in these cities at that time refutes this. In the city of San Antonio there occurred during these four months 49 cases, with 19 deaths, and in Galveston 192 cases. The civil population in these cities where our principal camps were located serve as a control, and show what would have happened without typhoid prophylaxis.

In the origin and spread of typhoid fever in our army during the Spanish-American War, investigated by a Board consisting of Reed, Shakespeare, and Vaughn,² they reported that in certain regiments of regulars the disease developed in three to five weeks, and that more than 90 per cent. of the volunteer regiments developed the disease within eight weeks of going into camp. Among the whole body of troops there were no less than 20,000 cases between May and September. The Second Division, Seventh Army Corps, assembled at Jacksonville, Florida, with 2,000 less in numbers than the Maneuver Division, for the same length of time, same latitude, with an equally good campsite, and an artesian water supply of absolute purity, had 1,729 cases of typhoid, with 248 deaths. As Colonel Kean remarks,³ "this division was not conspicuously unfortunate in its typhoid record for that time." It is selected for comparison on account of the close similarity of its conditions of service with those of the Maneuver Division.

This experience at the Mexican border with the Maneuver Division, so remarkable in its results, and so thoroughly convincing as to the value of vaccination against typhoid, resulted in the issuing of an order from the War Department making vaccination against typhoid compulsory in our army. This was the first instance of compulsory vaccination against typhoid as a requirement in an army. Up to October 30, 1911, 81,340 persons had been inoculated with prophylactic furnished from the Army Medical School. From the report of the Surgeon General, 1911, for the calendar years 1909 and 1910, only 11 cases of typhoid occurred among the inoculated, with no deaths, while in the non-inoculated part of the army there occurred 304 cases, with 26 deaths.

A comparison between the inoculated and non-inoculated parts of the army is shown by the fact that in 1910 the mean strength of the army numbered 76,230 American troops. Of this 17,978 had been given the typhoid prophylactic (about one-fourth of the army); only 7 cases occurred among the inoculated, with no

² Origin and Spread of Typhoid Fever during the Spanish-American War (1898), Harrington's Hygiene, p. 668

³ The Sanitary Record of the Maneuver Division, Jour. Amer. Med. Assoc., August 26, 1911.

deaths, whereas in the non-inoculated (three fourths of the army) there occurred 135 cases, with 10 deaths. It is not surprising that vaccination against typhoid falls short of giving immunity in some instances. As pointed out in the Surgeon General's report,⁴ there are no doubt persons who cannot be altogether protected against infection, just as vaccination against smallpox will not invariably protect against that disease. But the few mild cases, 11 in all, occurring in the inoculated, without a single death, is strong evidence that the disease was modified by the inoculations, although complete immunity was not obtained in these 11 cases.

Vaccination against typhoid as given in the army is administered hypodermically in three doses. The injections are given in the subcutaneous tissue of the left arm at the level of the insertion of the deltoid. The skin is prepared in the usual manner, by scrubbing with soap and water, followed by alcohol, then the skin is painted with a 5 per cent. tincture of iodine before and after the injection. The hypodermic syringe and needle are rendered sterile by boiling. The first dose contains 500,000,000 killed typhoid bacilli in $\frac{1}{2}$ c.c. of sterile salt solution. The second and third dose, each given at intervals of ten days, contain 1,000,000,000 bacilli in 1 c.c. of salt solution.

The injection is given in the afternoon about four o'clock. This in order that the effects of the reaction will wear off during the night. The immediate effect of the inoculation is a smarting pain lasting only for a minute or two, nothing further is noted until four or five hours afterward, when the man may have a headache and a feeling of malaise, and at the site of inoculation a red and tender area about the size of the palm of the hand.

The headache and other symptoms are rarely sufficient to interfere with sleep, and by next morning all symptoms have usually disappeared. Occasionally soreness is noted in the axillary region, and the lymph nodes may become slightly swollen and tender, but the swelling usually disappears in about twenty-four hours, and is never followed by permanent enlargement or suppuration. In over 100,000 injections in not a single case has a hypodermic abscess occurred. The complete immunity to abscesses is undoubtedly due to the small amount of trikresol (0.4 per cent.) used in preparing the vaccine. As an evidence of how slight the effects of the inoculations were regarded by the men, at my former station no difficulty was experienced by me in obtaining volunteers for inoculation to the extent of 90 per cent. of the command.

It is very interesting to note that persons who have suffered an attack of typhoid usually have the severer reactions. Sir W. B. Leishman expresses the opinion that an exceptional severity of

⁴ Report of Surgeon General of the Army, 1911, p. 50.

reaction indicates an unusual degree of susceptibility of the individual. So these are apparently cases of hypersensitiveness to infection. A case illustrating this happened in our service last year. A man who had typhoid in 1899 was inoculated in June 1909, receiving two doses. The first dose produced a moderate reaction, while an exceptionally severe one followed the second. In March, 1910, he had a mild attack of typhoid. The conclusion seems warranted that in this case we have an instance of individual hypersensitiveness to typhoid infection.

A few words as to the preparation of our vaccine, the nature and degree of immunity afforded, and the duration of such an immunity. The vaccine⁵ which has been used in the army has all been prepared at the Army Medical School at Washington. It has been prepared from a single strain of the bacillus which has been for many years under cultivation, and has practically lost its virulence for animals. It grows luxuriously on agar, and presents the usual characteristics on all laboratory media. Before making a batch the culture is plated out and half a dozen typical colonies are selected for further use. The growth on each of six tubes is washed off in 2 c.c. of broth, and used in the next step, which is the inoculation of a number of Kolle flasks. The cultures are incubated for eighteen hours, each flask carefully scrutinized for contamination, and the growth washed off in salt solution. The emulsion is collected in two liter flasks. The flasks are sunk in a water bath, and kept at 55° C. for one hour after the temperature of bath is reached.

While the flasks are in the bath the emulsion is standardized by counting the bacteria in a sample of the unkilld emulsion. The method is a modification of the one devised by Sir A. E. Wright. Equal parts of the normal human blood and emulsion to be counted are thoroughly mixed. Small drops of the mixture spread on slides are stained, and counts of both the red cells and the bacteria made in a large number of different microscopic fields. Since we know that normal human blood contains 5,000,000 red blood corpuscles per cubic millimeter, it is easy to count the actual number of bacteria from the ratio between the two.

On account of lysis occurring in some of the more delicate bacteria, Major Harrison, of the R. A. M. C., modified Wright's method by washing the red blood corpuscles free from their serum in sodium citrate before adding them to the bacteria. The ratio of bacteria to the red blood corpuscles is not disturbed by the washing of the latter, since they are equal in the beginning. The counts obtained from the broth cultures of the bacillus after forty-

⁵ Russell, New York State Journal, December, 1910 (this report has been drawn on very freely by the author, particularly laboratory technique, etc., as regards preparation of prophylactic).

eight hours' incubation run from 1,200,000,000 to 1,400,000,000 bacteria to the cubic centimeter, hence the stock culture must be diluted with salt solution until 1 c.c. contains approximately 1,000,000,000 bacteria. To the standard emulsion is added 0.25 per cent. trikresol, thus making it doubly certain that all the bacteria are killed. It is put up in sealed glass ampules. Each container is labelled with the name and number of the product, and given a date three months from the time of its preparation, after which it should not be used.

Investigations of blood changes following vaccination against typhoid were made by Pfeifer and Kolle in 1896. They showed, from a thorough and exhaustive study of the specific changes in the blood serum, that not only were agglutinins produced, but what is more important, that the bacteriolytic power of the blood was also raised in the same way as during an attack of typhoid. So far as is known at present we have, then, the same antibodies produced as a result of inoculation as are produced during clinical typhoid, and the quantity of agglutinins, bacteriolysins, and opsonins seems to be even greater after vaccination than after clinical typhoid, and it is therefore not unreasonable to expect that the immunity conferred by vaccination will last for a considerable period. From tests made at the laboratory of the Army Medical School of a large number of vaccinated persons, the Widal was invariably positive after vaccination, in many cases being present in dilutions of 1 in 5,000, 10,000, or even 1 in 20,000, and usually remaining present for nearly a year, in some instances for seventeen and twenty months.

As to the length of time immunity is offered after vaccination, this cannot be definitely answered at present, and until observation can be made over a prolonged period this question cannot be accurately determined. The present plan in the Army is to vaccinate every three years.

As modern wars are unlikely to last over three years, what an ideal agent we have for the control of the most dreaded camp disease. A disease which, during the short life of the Spanish-American war, claimed 20,738 victims, with 1,580 deaths, or 86.24 per cent. of the entire mortality of the war. The application of this prophylactic, so ideal for the army, is no less important to the nurse in training, the hospital attendant, the interne, the physician, and in the face of an epidemic, the community.

AN EXPERIMENTAL STUDY OF HIGH INTESTINAL OBSTRUCTION.

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INTESTINAL obstruction in man, if unrelieved, speedily causes death. The fatal outcome is too rapid to be the result of starvation, and three general theories have been advanced to explain it: (1) A disorder of the nervous mechanism controlling the cardiac and vasomotor systems. (2) A bacterial infection of the organism by the passage outward of bacteria from the intestinal lumen. (3) An intoxication from poisonous substances imprisoned in the intestine orally to the obstruction.

The advocates of these various theories have done a vast amount of experimentation to uphold one or the other, but up to the present time the question remains unsettled.

THE THEORY OF A NERVOUS DISORDER. In favor of the first theory, clinical evidence has been adduced. The tachycardia, the low blood pressure, the profound collapse of the patient, and the wide dilatation of the splanchnic bloodvessels all point to a loss of activity on the part of the medullary nerve centres. The early writers saw in these the result of a reflex disturbance from stimuli acting on the nerve endings in the intestinal wall. It is undoubtedly true, however, that exactly this train of events may arise from a toxemia or a bacteremia without the intervention of any afferent nerve impulses.

Recently, Braun and Boruttau,¹ have modified this theory somewhat, and assign the above symptoms to a disturbance of the circulation resulting from interference, chiefly mechanical, with the inherent nerve plexuses in the intestinal wall. They see a parallel between a gradual bleeding to death and the death in intestinal obstruction. The loss of body fluids resulting from failure of absorption, the enormous outflow of fluid into the intestine, the persistent vomiting, and the stagnation of blood in the splanchnic area lead to an anemia of the brain centres which progresses till these centres cease their activity, and death results. They experi-

¹ Deutsch. Zeitsch. f. Chir., 1908, xevi, S. 544.

mented most exhaustively on rabbits to support this view, but the evidence is all indirect, and seems to us not to amount to a proof of the absence of a toxemia. We are unable to find in the literature any experimental work which is convincing that the nervous system is primarily at fault. Certainly, as death approaches, there is a profound disturbance of the nervous control of the heart, bloodvessels, and respiration, but this, we believe, is in no sense a reflex disturbance, nor the result of an anemia, *per se*, of the nerve centres.

THE THEORY OF BACTERIAL INFECTION. The infection theory has much more to substantiate it. The intestinal lumen is the normal habitat of innumerable microorganisms which are potentially pathogenic. When an obstruction exists, these no longer have their normal outlet *per anum*. They are dammed up in the intestine under favorable conditions for their growth (McClure²). The damage to the intestinal mucosa may allow their passage outward, either into the blood stream, the lymphatics, or directly into the peritoneal cavity. Proof of this possibility is seen clinically in the presence of a peritonitis as a complication of intestinal obstruction without perforation; also in the frequent finding of the colon bacillus in the blood as a pathogenic microorganism, under very varied conditions of intestinal disturbances less severe than an obstruction, and in the bacteremia from the *Bacillus typhosus* when the intestine is ulcerated by the action of that organism.

Von Khantz,³ experimenting on rabbits in a low intestinal obstruction, often found a bacterial invasion of the blood and the peritoneum, but never the former without the latter. Borszesky and von Genersich,⁴ on the other hand, found a blood infection with no invasion of the peritoneum. There can be no doubt that a bacterial invasion of both the peritoneum and the blood may take place in intestinal obstruction, but it is not an essential accompaniment. It occurs late as a complication, often a terminal one. Both clinically and experimentally it will result most often when the obstruction is complicated by a strangulation. Without this complication, intestinal obstruction will kill with no passage of bacteria beyond their normal place of occurrence in the bowel lumen.

The tables on pages 362 to 363 give the result of our experiments bearing on this point. In the first series the obstruction was produced by dividing the intestine from 10 to 30 cm. below the pylorus, and closing the ends by inversion. It will be noted that in all these cases some microorganisms were found in the organs examined.

² Jour. Amer. Med. Assoc., 1907, xlix, 1003.

³ Arch. f. klin. Chir., 1909, xxxviii, p. 412.

⁴ Beiträge z. klin. Chir., Band xxxvi, S. 448.

This, we believe, was due to two factors, namely, the necessary local soiling of the peritoneum by the method of operating, and the fact that all the examinations were made several hours post mortem, because the animals died during the night. In the second series, however, the obstruction was produced by the clamp described below, and the animals were either killed when it was believed they were too sick to live over night, and immediately examined, or the examination was made very soon after the animal died from the obstruction itself. This series of 7 cases furnishes irrefutable proof that death results from an obstruction of the upper intestine in the dog, without any invasion of the peritoneum, blood, liver, or spleen by bacteria, which are demonstrable by the methods employed. The methods in the two series were exactly similar and their efficiency in detecting organisms is amply demonstrated in the first. The cultures were taken at autopsy on slant agar or Loeffler blood serum or both. Usually four tubes, sometimes only three of each were inoculated from each tissue, and grown under both aërobic and anaërobic conditions at incubator temperature. For the anaërobes the Buchner method or the Cornell modification of it was used. The tubes were examined at the end of one, two, and three days. All the cultures were made in the sterile room of the Cornell bacteriology laboratory. This consists of a closed cabinet, ventilated through a bacterial proof filter, in the roof of which is suspended an ordinary revolving lawn sprinkler. The water is turned through this for fifteen or twenty minutes prior to taking the cultures. Thus the air is mechanically sterilized by washing out the microorganisms. All the needed apparatus for taking the cultures and smears is assembled before beginning the inoculations, and the air-tight door is kept closed until all cultures are completed. The technique in making the inoculations is that usually employed in obtaining cultures from postmortem material. The efficiency of the room and the method is demonstrated by the fact that only three air contaminations were found in several hundred tubes.

In some of the later cases of the second series no cultures were taken from the spleen, since it was noted that this organ never showed infection when the liver and peritoneum were without infection. Often, too, the spleen cultures gave no growth when the other organs were actively infected. A summary of this series shows that the femoral blood was cultured seven times and always was without growth; the liver was cultured six times, and showed one colony of Gram-positive cocci, in one tube of one case, probably an air contamination; the results from the peritoneal cultures were exactly the same as from the liver; the spleen was cultured only twice, with negative findings both times; the jejunal or duodenal contents above the clamp were cultured seven times, and all tubes showed an abundant growth of various microorganisms.

SERIES I

Case.	Organs.	Cultures taken.	Tubes showing cocci.	Tubes showing bacilli.	Characteristics.	Remarks.
12	Spleen	2 aerobic 3 anaerobic	None	1 aerobic 2 anaerobic	Morphology and growth characteristic of colon bacillus on usual differential media	Intestine sectioned and closed 34 cm. distal to pylorus. Lived eighty hours. Cultures taken ten hours postmortem.
	Liver	2 aerobic 4 anaerobic	All	All	(1) Gram + coccus. (2) Bacillus identified as colon on differential media. (3) Also very many colonies of a large gram + anaerobic bacillus with morphology of bacillus aerogenes capsulatus.	
	Jejunum	2 aerobic 4 anaerobic	All	All	(1) Gram + coccus. (2) Large anaerobic Gram + bacillus. (3) Gram - bacillus of two kinds, first long and slender; second, short and plump. Both grew in anaerobic tubes, while the former only grew in aerobic tubes.	
13	Femoral blood	4 aerobic 4 anaerobic	None	None		Intestine sectioned 36 cm. from pylorus and ends closed. Autopsy about thirteen hours post-mortem.
	Peritoneum	4 anaerobic	4 aerobic	None	(1) Gram + and (2) Gram - coccus.	
	Spleen	4 aerobic 3 anaerobic	1 aerobic	None	Gram + coccus. Same organism as in peritoneum.	
	Liver Jejunum	4 each 4 each	None All	None All	Same as in Case 12.	
14	Jejunum at operation	2 aerobic 2 anaerobic	All	All	(1) Gram negative bacillus. (2) Gram + coccus. (3) Large Gram + bacillus	Intestine sutured after section 31 cm. from pylorus. Autopsy thirty-six hours post-mortem.
	Jejunum at autopsy	4 each	All	All	(1) Anaerobic gas forming Gram - bacillus. (2) Gram + bacillus. (3) Gram + coccus.	
	Femoral blood	4 each	2 aerobic	All	(1) Gram positive coccus, ferments lactose, and glucose, without gas, no change in neutral red and safranin. (2) Large anaerobic Gram + bacillus with morphology of aerogenes capsulatus bacillus.	
	Peritoneum	2 each	All	All	(1) Gram + coccus, same as in femoral blood. (2) Gram - bacillus-like colon. bacillus.	
	Spleen	4 anaerobic 4 aerobic	2 aerobic	2 anaerobic	(1) Gram - coccus. (2) Gram - bacillus having the characteristics of coli communis.	
	Liver	2 anaerobic 4 aerobic	2 anaerobic 3 aerobic	None	(1) Gram + coccus as in peritoneum and femoral blood.	

Case.	Organs.	Cultures taken.	Tubes showing cocci.	Tubes showing bacilli.	Characteristics.	Remarks.
15	Jejunum at operation	4 each	4 anaërobic	4 anaërobic 2 aërobic	Gram — bacillus, mobile same as in peritoneum.	Intestine ligated with tape 35 cm. from pylorus. Autopsy four hours post mortem. General peritonitis present.
	Jejunum at autopsy	4 each	1 anaërobic	4 anaërobic 4 aërobic	(1) Gram — bacillus having characteristics of colon bacillus (2) Gram—bacillus intermediate in colon group, changes neutral red and safranin, does not ferment lactose. (3) Gram + coccus.	
	Peritoneum	4 each	4 anaërobic	4 anaërobic 4 aërobic		
16	Femoral blood	4 each	None	None	Not identified	Bowel sectioned and inverted 48 cm. from pylorus. Lived about thirty-two hours. Autopsy twelve hours post mortem. No peritonitis.
	Spleen	4 each	None	None		
	Liver	4 each	None	None		
	Jejunum at operation	4 aërobic 4 anaërobic		4 anaërobic 4 aërobic		
	Jejunum at autopsy	4 aërobic 4 anaërobic	4 anaërobic 4 aërobic	4 anaërobic 4 aërobic	(1) Short Gram — bacillus. (2) Gram + coccus resembling streptococcus. (3) Large Gram + bacillus.	
17	Femoral blood	4 aërobic 4 anaërobic	None	None	Gram — short, stout, bacillus mobile (2 strains), resembling colon bacillus. (2) Gram + bacillus. (3) Gram + coccus.	Jejunum clamped 37 cm. from pylorus with Crile clamp, which at autopsy was found to have cut through. Autopsy eight hours post mortem, lived about eighty-eight hours. General peritonitis present.
	Spleen	4 aërobic 4 anaërobic	None	None		
	Liver	4 aërobic 4 anaërobic	4 anaërobic 4 aërobic	4 anaërobic 4 aërobic	(1) Gram + coccus. (2) Gram + bacillus. (3) Gram — bacillus, short and stout, mobile. Same as in liver.	
	Peritoneum	4 aërobic 4 anaërobic	4 anaërobic 4 aërobic	4 anaërobic 4 aërobic		
	Jejunum at autopsy	None taken	None taken	
	Femoral blood	4 aërobic 4 anaërobic	None	None	Gram + coccus. One colony outside line of inoculation. Probable air contamination.	
	Spleen	4 aërobic 4 anaërobic	1 anaërobic	None		
	Liver	4 aërobic 4 anaërobic	None	None	(1) Gram — bacillus, having characteristics of coli communis. (2) Gram + coccus. (3) Gram + bacillus short and fat and growing in long chains.	
	Peritoneum	4 aërobic 4 anaërobic	4 anaërobic 3 aërobic	4 anaërobic 3 aërobic		

Case.	Organs.	Cultures taken.	Tubes showing cocci.	Tubes showing bacilli.	Characteristics.	Remarks.
18	Jejunum	None taken	Jejunum clamped with Crile clamp 20cm. from pylorus. Killed with chloroform ninety-one hours after operation. Clamp cut through, local peritonitis resulting.
	Femoral blood	4 aerobic 4 anaerobic	None	None		
	Peritoneum	4 aerobic 4 anaerobic	None	4 anaerobic 4 aerobic	(1) Gram - bacillus. (2) Gram + bacillus.	

SERIES II.

19	Jejunum	3 aerobic 3 anaerobic	3 anaerobic	3 anaerobic 3 aerobic	(1) Gram - bacillus. (2) Gram + coccus.	Intestine occluded with special clamp 18 cm. from pylorus. Lived one hundred and seventy-two hours after operation. Killed with chloroform. Autopsy immediately. No peritonitis; local abscess around clamp.
	Femoral blood	4 aerobic 3 anaerobic	None	None		
	Spleen	4 aerobic 4 anaerobic	None	None		
	Liver	4 aerobic 3 anaerobic	None	None		
	Peritoneum	3 anaerobic 4 aerobic	None	None		
	Abscess around clamp	2 aerobic 2 anaerobic	1 anaerobic 2 aerobic	Gram negative bacilli.	
20	Jejunum	None taken	Occlusion clamp 16 cm. from pylorus. Lived ninety hours. Died. Autopsy. No peritonitis.
	Femoral blood	4 aerobic 4 anaerobic	None	None		
	Liver	4 anaerobic 4 aerobic	None	None		
	Peritoneum	4 anaerobic 4 aerobic	None	None		
	Exudate around clamp	3 aerobic 3 anaerobic	None	None		
21	Jejunum	4 aerobic 4 anaerobic	4 anaerobic 4 aerobic	4 anaerobic 4 aerobic	(1) Gram + coccus. (2) Gram + bacillus. (3) Gram - bacillus.	Occlusion clamp on jejunum 16 cm. from pylorus. Dog lived 58 hours. Autopsy 8 hours post mortem. Peritoneum clean.
	Femoral blood	4 aerobic 4 anaerobic	None	None		
	Spleen	4 aerobic 4 anaerobic	None	None		
	Liver	4 aerobic 4 anaerobic	None	None		
	Peritoneum	3 aerobic 4 anaerobic	1 aerobic	Gram + coccus. One colony only, probably air contamination.	
22	Jejunum	3 aerobic 3 anaerobic	2 aerobic 1 anaerobic	Gram + cocci	Occlusion clamp 12 cm. from pylorus. Lived twenty-one days. Killed with ether. Clamp not absolutely tight. No peritonitis.
	Femoral blood	4 aerobic 4 anaerobic	None	None		
	Liver	3 aerobic 3 anaerobic	None	None		
	Peritoneum	4 aerobic 4 anaerobic	None	None		

Case.	Organs.	Cultures taken.	Tubes showing cocci.	Tubes showing bacilli.	Characterisitic.	Remarks.	
23	Jejunum	None taken	Occlusion clamp 12 cm. from pylorus. Lived two hundred and forty hours. Killed with cyanide and autopsied immediately. No peritonitis. Clamp tight.	
24	Femoral blood	3 aërobic 3 anaërobic	None	None	Gram positive and negative bacilli	Occlusion clamp 16 cm. from pylorus. Lived two hundred and five hours. Autopsied two hours post mortem. No peritonitis. Small abscess around clamp which was tight.	
	Peritoneum	4 aërobic 4 anaërobic	None	None			
26	Jejunum	2 aërobic 2 anaërobic	2 aërobic 2 anaërobic	Pure growth of Gram + coccus. (1) Small Gram negative bacillus. (2) Large, long Gram + bacillus	Occlusion clamp 16 cm. from pylorus. Lived two hundred and forty hours. Killed with ether. Autopsy immediate. No peritonitis.	
	Femoral blood	3 aërobic 4 anaërobic	None	None			
	Liver	4 aërobic 4 anaërobic	None	None			
	Peritoneum	4 aërobic 4 anaërobic	None	None			
	Clamp Abscess	2 aërobic 2 anaërobic	2 anaërobic 2 aërobic			
	Jejunum	4 aërobic 4 anaërobic None	4 aërobic 4 anaërobic			
28	Femoral blood	4 aërobic 4 anaërobic	None	None	One colony outside inoculation of a Gram positive coccus.	Occlusion clamp 11 cm. from pylorus. Lived fifty-six hours. Autopsy ten hours post mortem. Abscess around clamp. No peritonitis. Clamp tight.	
	Liver	3 aërobic 4 anaërobic	1 aërobic	None			
	Peritoneum	4 aërobic 4 anaërobic	None	None	Gram positive and negative bacilli and negative cocci. Anaërobic tubes show gas production.		
	Jejunum	2 aërobic 2 anaërobic	2 anaërobic	2 aërobic 2 anaërobic			
	Femoral blood	4 aërobic 4 anaërobic	None	None			
	Liver	4 aërobic 3 anaërobic	None	None			
	Peritoneum	4 aërobic 4 anaërobic	None	None			
	Clamp abscess	2 aërobic 2 anaërobic	None	None			

Case 22, is not included in the above summary because the obstruction was not complete. It is worthy of note here, however, that the jejunal tube only showed a growth of a Gram-positive coccus in one-half the tubes inoculated, showing that the long period (twenty-one days) with only sterile water by mouth did much toward sterilizing the upper bowel.

THE INTOXICATION THEORY. This theory has experimental evidence to support it, and no experiments have proved the absence of a toxemia. Clairmont and Ranzi⁵ demonstrated that the stagnated material above an obstruction, after passage through a Reichel or Pukal filter, was exceedingly toxic when injected into the blood of an animal. Kukula⁶ found a toxic material in the alcoholic extracts of the intestinal contents in experimental ileus. Roger,⁷ and Roger and Garnier⁸ went farther and proved that the normal content of both the stomach and the intestine are poisonous when thus injected. They did not filter it, but death occurred too early to be the result of an infection. The toxicity was only one-third as great when injected into the portal vein as when injected into a peripheral vein. They also injected it into a mesenteric artery, against the current, so that it was carried backward and then redistributed through branches to a considerable section of the intestine. Here it produced emboli and stopped the absorption, so that large doses were not fatal. This power to cause clotting in the vessels of the intestine is mentioned in this connection because it may account for the gangrene resulting in some of our experiments (see page 386). Murphy and Vincent⁹ found the material from the obstructed or strangulated intestine very poisonous when injected into the peritoneal cavity, and that its poisonous properties were destroyed by boiling or passage through a Berkefeld filter. They concluded, therefore, that living bacteria are the important factors. It does not seem to us that this conclusion is tenable. Their experiments only prove that living bacteria, if they obtain entrance into the peritoneum, will kill. They do not disprove the presence of other poisons in the obstructed intestine, which, being slowly absorbed over a period of some hours, or days, will kill with the symptoms of ileus. Such poisons may be constantly elaborated and absorbed, but may never be present at any one time in sufficient quantity to cause death when injected into the peritoneal cavity. The symptoms arising from the injection of the intestinal contents into the blood, as reported, differ very markedly from those appearing in the obstructed animal, and there are many objections as pointed out by Guibe,¹⁰ Braun and Boruttau,¹¹ Korentchevsky,¹² and others, against accepting these experiments as directly bearing on the cause of death in intestinal obstruction. The lessened absorption from the obstructed intestine is one objection offered. Clairmont and

⁵ Archiv f. klin. Chir., 1904, Band lxxiii, S. 696.

⁶ Ibid., Band lxxiii, S. 773.

⁷ La Revue Scientifique, January 19, 1907, vol. i; La Presse Médicale, January 4, 1911.

⁸ Archiv. de med. Experiment, July, 1906; Revue de Médecine, August 10, 1906; La Presse Médicale, May 23, 1906.

⁹ Boston Med. and Surg. Jour., November 2, 1911.

¹⁰ La Presse Médicale, April 3, 1909.

¹² Roussky Vratsch, 1908, p. 1572. (Cited by Guibe.)

¹¹ Loc. cit.

Ranzi¹³ found that potassium iodide placed in the bowel above the obstruction, was excreted from the kidneys in greater quantities than normal, up to eight or ten hours after the obstruction was produced, the excretion rapidly decreased after that, and came to a stop in about fifteen hours. Braun and Boruttau¹⁴ gave strychnine to their obstructed animals, and from the resulting symptoms they concluded that absorption became markedly reduced from the start. On this experiment they base their chief objection to the intoxication theory. However, as we shall show in our experiments, the development of symptoms is very slow, and death, under proper precautions to exclude damage to the intestinal wall, may be long postponed, so that a minimal absorption of poison is all that is required. A more important objection, than the lessened absorption, to using the evidence of the injection experiments as a proof of the intoxication theory, is that many substances injected directly into the circulation are poisonous, whereas, if they have to pass through living cells to get into the blood, their poisonous properties are entirely destroyed. Peptone is such a substance, and is a good illustration in this connection. The injection of peptone into the blood produces symptoms of poisoning, which may end in death. The absorption of peptone from the intestine is, on the contrary, a normal physiological process. Therefore, the mere presence of substances in the obstructed intestinal tract, which act as poisons when injected into the blood, is no indication that these substances cause the death resulting from an obstruction, since they are normally found in the intestine in conditions of continued health. To accept the view that such a death results from a toxemia it must be conceived either that new poisons are elaborated and absorbed or that an abnormal absorption of the poisons normally present takes place. In undertaking our work, after a study of the literature, we tentatively accepted the first hypothesis and planned our experiments to determine by a process of exclusion from what sources such new poison or poisons arise. In this endeavor we were only partially successful, but as the work developed the second conception was forced upon us, namely, that the essential factor in causing the symptoms and death in intestinal obstruction does not lie in the poisons *per se*, but in the production of lesions which favor their abnormal absorption. We believe our readers will get a clearer understanding of our findings if he will follow, step by step, the reasoning and experiments which led to this change of conception in our minds.

In searching for the source of the poison we accepted three possibilities: (1) Foodstuffs or substances derived from them; (2) true bacterial toxins; (3) secretory substances from the ali-

¹³ Loc. cit.

¹⁴ Loc. cit.

mentary tract and digestive glands, or their derivatives. It was our intention to exclude one after the other of these possible sources and study the conditions resulting after an obstruction was produced. It is readily conceivable that there may enter into all of these the result of bacterial activity. While, as detailed above, our experiments have shown that a bacteremia is not necessarily present, they have not excluded either a bacterial toxin or substances developed by virtue of the presence of bacteria in the occluded bowel. Indirectly, however, there is some clinical and experimental evidence that bacteria are not an essential in the process. Clinically, we know that a high obstruction produces much more severe symptoms, and is more rapidly fatal, than a low obstruction. The bacteria, however, are much more numerous in the lower bowel than in the upper. Roger and Garnier¹⁵ found the most toxic substance in the duodenum; the least in the colon. The toxicity, too, was greater in unobstructed conditions, than in the obstructed conditions, and it grew less the longer the obstruction continued, while McClure¹⁶ has shown that the bacteria increase rapidly when an obstruction is produced. Vidal¹⁷ found that the toxicity could be decreased by injecting, simultaneously with the duodenal contents, glycerin extract from the jejunal mucosa lower down, and this cannot be explained on the ground that bacteria are the exciting cause of the poison. V. Baracz¹⁸ found that dogs with a double occlusion of the lower ileum and cecum might live for many weeks. At the end of this time only a moderate quantity of material was found in the loop. The contents were rich in bacteria. The intestinal wall showed marked changes; mostly in the form of an hypertrophy, but sometimes an atrophy was present. The microscopic findings are not given. In one case the animal was killed after four hundred and twenty-five days while in a condition of perfect health. Here the bowel loop, about 20 cm. in length, was found enormously distended, filled with 365 grams of a foul-smelling, greenish material, which was rich in bacteria; a bacillus, the *Bacterium aërogenes* and a leptothrix being isolated in cultures. These cases seem to point to the conclusion that the stagnation of bacteria and their toxins in the intestine is not sufficient to cause the symptoms seen in intestinal obstruction. Indeed, they, with the facts cited immediately above, seem to make it doubtful whether microorganisms play any essential part, either directly or indirectly, in producing these symptoms. This question, however, must remain an open one for the present, and the writers can offer no positive answer to it.

There still remain the stagnated foodstuffs, and the stagnated glandular secretions of the stomach, intestine, liver, and pancreas

¹⁵ Loc. cit.

¹⁷ *Revue de Chir.*, October 10, 1900, xxii; *Congres. Francais de Chir.*, 1905, xxviii, 1237.

¹⁸ *Archiv f. klin. Chir.*, Band lviii.

¹⁶ Loc. cit.

as the source of the poisonous materials. Draper,¹⁹ of Rochester—formerly Maury of New York—has worked on the theory that the duodenum secretes a substance or substances which normally are rendered non-toxic by passing over the jejunal mucous membrane lower down. When obstruction is present the duodenal substances are not brought into contact with the antibodies, and, hence, remain poisonous and cause death. Vidal earlier advanced this view.

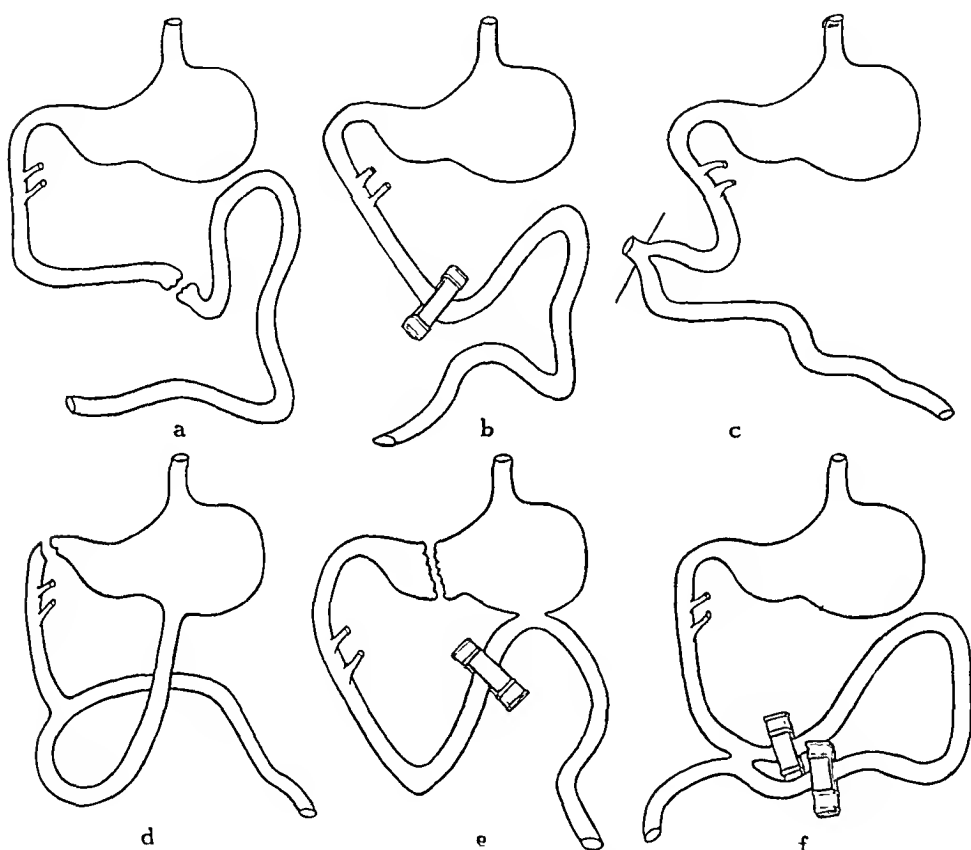


FIG. 1.—Showing the types of operation done: *a*, obstruction by sectioning and inverting the cut ends; *b*, obstruction by means of the special clamp; *c*, attempt to produce sterile condition of gut by fistula and washing; *d*, elimination of duodenal contents from upper bowel; *e*, double occlusion of one-half of the stomach and the duodenum with reestablishment of the alimentary canal; *f*, the same in the small intestine distal to the duodenum.

Draper has done some elaborate experiments in the way of side-tracking the various secretions to support this theory, but his reports are somewhat contradictory, and he himself says very inconclusive. Recently he has reported that feeding dogs which have an obstruction just distal to the duodenum, with the excised mucous membrane from the jejunum and ileum of other dogs,

¹⁹ Jour. Amer. Med. Assoc., October 21, 1911; Johns Hopkins Hosp. Bull., 1909, p. 838; AMER. JOUR. MED. SCI., vol. cxxxvii, p. 725, and Jour. Amer. Med. Assoc., 1910, liv, 5.

prolongs the life of the obstructed dogs. The difference between the control dogs and the fed dogs, however, was not marked, and the exceptions where a fed dog died in a shorter time, or one not fed lived a longer time, were too numerous to make the total result at all convincing.

The possible relation of the stagnated foodstuffs to the production of the poisons was studied in the following experiments. The type of operation is shown in Fig. 1.

EXPERIMENTS.

All animals were fully etherized before operation. No food was given in any case after the operation, unless so stated. Water, however, was given freely, unless otherwise noted.

No. 3. A cat which had received no food for ninety-six hours before operation. Duodenum sectioned and ends closed by inversion 10 cm. below pylorus. For three days the animal remained in good condition. Vomited. Fourth day showed marked weakness and some rigidity of muscles of extremities. Just before death had convulsions involving extremities. Killed with chloroform ninety-six hours after obstruction. Autopsy immediate. No peritonitis. Closure of bowel ends tight. Stomach contained small amount of normal appearing gastric content. Duodenum empty. Neither stomach or duodenum was distended.

No. 4. Fox terrier. Fed twenty hours before operation. Repetition of No. 3, the section being 11 cm. distal to the pylorus. Except for some weakness and vomiting, seemed like normal dog for four days. Died with progressive weakness and vomiting on seventh day. Autopsy. No intestinal leakage. No peritonitis. Stomach slightly distended. Duodenum not distended.

No. 5. Bitch. Weight 9.8 kgr. Fed last time forty-eight hours before operation. Repetition of No. 3. Post-operative course the same. Lived one hundred hours. Autopsy. No intestinal leakage. No peritonitis. No distention of stomach or duodenum.

No. 6. Bitch. Weight 10.85 kgr. Starved for seventy-two hours. Repetition of No. 3, section being 12 cm. below pylorus. Post-operative course the same. Temperature varied from 36.6° to 39° C. Lived for fifty-five hours. Autopsy. Same findings as those given above.

No. 7. Dog. Weight 19.7 kgr. Fed last time forty-eight hours before operation. Same operation 16 cm. below pylorus. Some peritoneal soiling with intestinal contents. Post-operative course same as others, except more acute. Temperature as high as 39.9° C. Lived only thirty-six hours. Autopsy yielded same findings as others.

No. 8. Dog. Medium weight. Fed six hours before operation. Same operation 12 cm. below pylorus. Post-operative course the same. Temperature 39°. Lived one hundred and eighteen hours. Autopsy. Same findings and in addition there were noted three superficial areas in the duodenum which resembled ulcers.

No. 9. Leakage of intestinal contents at closed end of proximal gut.

No. 10. Same.

No. 11. Dog. Weight 5.3 kgr. Fed twenty-six hours before operation. Same operation 33 cm. below pylorus. Lived only ten to fourteen hours. Autopsy. No leakage. No peritonitis. Stomach was not distended. Mucosa showed small punctate hemorrhages. Intestine proximal to section and for 80 cm. distal to it was much congested and showed hemorrhagic areas in it. We are unable to explain these last postmortem findings as being the result of the operation. Our belief, however, is that the early death resulted because of them.

No. 12. Bitch. Weight 9.2 kgr. Fed twenty-six hours before operation. Same operation 36 cm. below pylorus. Post-operative course as above. Lived eighty-two hours. Autopsy. Same findings as in other cases.

No. 13. Dog. Weight 8.2 kgr. Fed twenty-six hours before operation. Bowel sectioned 36 cm. below pylorus and ends inverted. Symptoms same as others. Temperature 35.5° C. Pulse 180 after twenty-four hours. Lived thirty-eight hours. Autopsy. No peritonitis. Ends of bowel tight. At distal closure an intussusception 14 cm. long had taken place and the intestinal wall was much damaged. This, we believe, contributed to early death.

No. 14. Young dog. Weight 5.75 kgr. Fed seven hours before operation. Bowel sectioned and ends inverted 31 cm. below pylorus. Never fully recovered from operation and died in twelve hours. Autopsy. No peritonitis. Closed ends tight.

No. 15. Dog. Weight 10.5 kgr. Fed forty-eight hours before operation. Bowel sectioned and ends closed 48 cm. below pylorus. Post-operative symptoms same as in other dogs. Lived thirty-two hours. Autopsy. No peritonitis. Closed ends tight; 10 cm. intussusception of distal end in gut, with much damage of gut wall. Proximal intestinal mucosa showed much congestion and many punctate hemorrhages.

These animals were operated upon at varying periods after eating, and none was fed anything after operation. The one which lived the longest, one hundred and sixty hours, was fed twenty hours before operation, and the one that died in ten hours was fed the last time twenty-seven hours before operation. One dog which ate a full meal only six hours before operation lived one hundred and sixteen hours, while one that had fasted for seventy-two hours lived fifty-five hours after operation. The dogs had

all the water, both before and after the operation, that they would take.

This same lack of correspondence between the state of digestion at the time the obstruction was produced on the one hand, and the severity of the symptoms and length of life afterward, was noted in all subsequent experiments. It seems, therefore, reasonably certain that decomposition of food residues in the tract has little to do with causing death, although the ingestion of food after the obstruction might readily be a factor.

The condition of the dogs after operation can be very briefly summarized. They showed a remarkable absence of active symptoms. Recovery from operation was usually prompt and complete, and on the next day they seemed well, but less lively than before. There was a slight rise in temperature. Water was drunk freely, and promptly vomited, washing out bile and mucus. Emaciation was marked. After a varying time the animal began to grow weak, but there was a lack of many of the symptoms we are accustomed to see in the human subject. Vomiting, as a rule, took place only after drinking. There was no abdominal distention, and no sign that cramps or colic were present. Once or twice we noted some rigidity of the muscles of the hind legs, as described by Maury, but in most cases no such rigidity could be demonstrated.

An autopsy was done in every case, and in none was there any gross alteration in the organs that accounted for death. The peritoneum was not inflamed. The stomach and the intestine above the section were never markedly distended. They usually contained only a very small amount of bile and mucus. The mucosa showed a severe congestion. In one or two cases there was a superficial ulceration in the intestinal mucosa. We were struck with the fact that the most severe changes of this character were present in the dogs living the shortest time. The gall-bladder was not distended. The kidneys and liver showed congestion, and the former evidence of degeneration.

From these cases it was determined that animals with a high obstruction might live as long as five to seven days; that the length of life was not dependent on the presence of food residue in the tract above the obstruction, and that autopsy gave no gross evidence of the cause of death. A complete microscopic study of these cases was not made. Where sections were examined, however, the same lesions were found in the intestinal mucosa, the kidney and the liver, as those to be described in the second group of cases.

We next turned our attention to the production of an obstruction which should not be complicated by any operative damage to the intestinal wall. This was considered advisable because there seemed to be a direct relation between the severity of this damage on the one hand, and the severity of the symptoms and

the early death of the dogs on the other (Nos. 11, 13, 15). In one case the bowel was closed by tying a tape around it and burying this with a row of Lembert sutures. The tape cut through and a perforative peritonitis followed. The same thing resulted in two cases where the Crile carotid clamp was used.

A special clamp was then devised, which proved to be efficient in causing a complete obstruction, without opening the gut, or damaging the blood supply. The clamp consisted of two rubber-covered aluminum plates, about 1 cm. in width and 4 cm. long. Over each end a second covering of rubber tubing was placed. One plate was then passed through a slit in the mesentery, with the bowel passing over it. The second plate was placed across the bowel at this point, and the two plates bound together near their ends. The interval left between them because of the rubber coverings over the ends allowed sufficient room for the intestine, tightly compressed, but not strangulated, to pass through. By bending the plates in or out the degree of obstruction was accurately regulated. We found by experience that the proper degree was obtained when the thin handle of a scalpel could just be passed within the bite of the plates, but not through it. (See Fig. 1, *b*.)

No. 19. The first dog on which the clamp was used was a male, weighing 13.5 kgm. He had been in the laboratory seventy-two hours without feeding, and had been given only sterile water to drink. This was done with the idea of getting the stomach and upper intestine as nearly free from bacteria as possible. Cushing and Livingood²⁰ have shown that the number present can be reduced very markedly in this way. The clamp was placed 18 cm. below the pylorus. The dog remained in excellent condition for five days following the operation. The temperature ranged from 37.5° to 38.5° C. and the pulse from 132 to 150. He drank freely of sterile water, which he vomited soon afterward, washing out bile and mucus with it. He passed small quantities of urine, which contained traces of bile and albumin. During this period he lost 1.8 kgr. He showed no active symptoms of the disease, and was in no apparent pain. The abdomen was not tender to palpation, nor was it distended. At operation the circumference of the abdomen was 47 cm. and on the fifth day only 43 cm. After the fifth day he began to show marked weakness and a more rapid loss of weight. The pulse and temperature remained about the same, and no new active symptoms developed. On the seventh day he was markedly weak and walked with difficulty. Emaciation was marked, there having been a loss equal to 19 per cent. of his body weight. He was killed with chloroform one hundred and seventy-two hours after the operation and the autopsy, with bacterial examination, immediately done.

The obstruction was tested under water pressure, and was found complete, no water passing through the clamped point. Coils of intestine and omentum were matted around the clamp. On separating these, a small local abscess of green odorless pus was opened. The peritoneal coat of the intestine, at this point, was eroded by pressure, but no serious damage was done to the rest of the wall. The general peritoneal cavity was entirely free from evidence of inflammation. The liver and kidneys showed a marked congestion. There was a marked dilatation of the stomach and upper intestinal segment, and both contained water with bile and mucus. Their mucosæ were markedly congested.

Microscopic Examination. The intestine proximal to the clamp shows intense congestion and considerable exudative inflammation of the subserous tissue. The submucosa shows hemorrhagic and leukocytic infiltration. There is an acute hyperplasia of the lymph follicles. Distal to the clamp the intestine is normal. The kidneys show intense capillary congestion, especially of the glomeruli. The epithelium is not well preserved.

The spleen shows congestion.

The pancreas is normal.

The liver sections were unsatisfactory.

The cultures from the abscess around the clamp showed a pure culture of a Gram-negative bacillus, having the characteristics of colon bacillus. Cultures taken from the inside of the intestine, just above the clamp, showed the same bacterial growth, and in addition, a gram-positive coccus. Our effort to sterilize the upper bowel was not successful, and the local abscess probably resulted from the passage of organisms outward through the intestinal wall, where the peritoneal coat was damaged by the clamp pressure. Other organs were sterile (see table).

No. 20. Dog. Weight 9.5 kgr. No food for one hundred hours. Sterile water during this time. Repetition of No. 19. Post-operative symptoms the same. Lived ninety hours. Autopsy (five hours postmortem during which time the body was on ice) showed no peritonitis. Obstruction complete. Stomach a little dilated. Bowel above clamp twice the normal size. In the intestine, distal to the clamp were seen many hemorrhagic points.

Microscopic Examination. Intestine proximal to clamp shows fibrinous peritonitis, marked congestion of all coats, and exfoliation of lining mucosal cells. Stomach normal.

Liver. Congestion. Moderate granular and fatty degeneration.

Kidney. Moderate congestion. Tubules show granular coagulum. Cells swollen and show marked granular degeneration. Some cells show partial necrosis.

Cultures from femoral blood, peritoneum and liver show neither aerobic nor anaerobic growth.

No. 21. Puppy. Weight 8 kgr. Fed four hours before operation. Clamp applied 16 cm. below pylorus. The stomach contained food and the lymphatics and vessels were distended from full digestion. The post-operative course was the same as in the others. Pulse, 190. Temperature, 39° C. He died fifty-eight hours after operation. Autopsy, eight hours post mortem, the body being on ice. No peritonitis. Moderate distention stomach and duodenum. Few drops of purulent looking fluid around clamp, buried in adhesions. The obstruction was complete. The gastric and intestinal mucosa, proximal to the clamp, showed very little change. Distal to the clamp there were areas which resembled submucous hemorrhages in the intestinal wall. The other abdominal organs appeared normal.

Microscopic Examination. Proximal intestine not examined. Distal intestinal mucosa shows hyperplasia of lymph follicles, but no hemorrhages.

Liver. Marked congestion.

Kidney. Congested. Tubule cells swollen, and in places intensely degenerated. Apparent necrosis present in some foci of the tubules.

Spleen and pancreas much congested.

Bacteriology. Cultures from femoral blood, peritoneum and liver all sterile, both aerobic and anaerobic, with exception of one colony on one peritoneal aerobic slant agar tube. This showed pure growth of a Gram positive coccus and probably was an air contamination, one of the three found in the whole series.

No. 22. Bitch. Weight 10.25 kgr. Fed eighteen hours before operation. Clamp applied 12 cm. below pylorus. This animal was killed on the twenty-first day, up to which time she had showed no symptoms of suffering or of disease, except for loss of weight to 7.4 kgr. During this time she had eaten nothing. She drank water freely, however, for the first three days. After this she received 150 to 250 c.c. of normal saline solution subcutaneously, and then she refused water to drink. She only occasionally vomited. The temperature ranged between 37° and 38° C. The pulse for the first four days was around 130. It then became slower and during the last two weeks was between 70 and 100. Urine was passed freely and contained bile and albumin in small quantities. Several blood-cell counts were made during the later days of the experiment and the red cells numbered between 5,240,000 and 7,000,000, nearly all counts being slightly over 5,000,000. Killed with ether on the twenty-first day while still in good health. Autopsy. No peritonitis. Clamp allowed minimal drainage into gut below (compare No. 27). Stomach and duodenum were somewhat dilated and the intestine distal to clamp was contracted, showing very little flow into it. However, it contained bile, and under pressure water was forced through clamp into

bowel below. The mucosa of intestine and stomach appeared normal. The kidneys and liver showed congestion.

Microscopic Examination. Stomach and intestine not examined.

Kidneys. Tubules filled with granular coagulum. Cells show swelling and granular degeneration.

Liver. Intensely congested.

Spleen. Congested.

Pancreas. Normal.

Bacteriology. Neither aërobic nor anaërobic growth on tubes from femoral blood, liver or spleen.

No. 23. Dog. Weight 11 kgr. Starved five days, receiving only sterile water. Clamp applied 20 cm. below pylorus. He was killed on the tenth day. His symptoms were the same as in cases above. He received saline subcutaneously with apparent benefit. Pulse, 132 to 150. Temperature, 37.9° to 39.2° C. Weight at death 8.5 kgr. Urine contained albumin and bile. An extensive noma developed on face which accounted for high temperature. Autopsy immediately after death by cyanide. Obstruction complete. Stomach and proximal gut much dilated. Distal gut collapsed (Fig. 3). They contained about 300 c.c. of bile, mucus, and water. The specimen was preserved intact so the mucosa was not seen. No peritonitis. Liver and kidneys much congested. The latter showed acute degeneration, the markings being indistinct and the papillæ pale.

Microscopic Examination. Kidneys show granular degeneration, in places very marked.

Liver. Intensely congested. Considerable fatty and granular degeneration.

Spleen and pancreas show congestion.

Bacteriology. Aërobic and anaërobic cultures from femoral blood and liver were all without growth.

No. 24. Small bitch. Weight 6 kgr. Fed seventy-two hours before operation. Clamp applied 16 cm. below pylorus. Lived two hundred and five hours—a little less than nine days—with symptoms as in other cases. Pulse, 120 to 180. Temperature average, 39° C. Received saline injections throughout. Red-blood cells increased from 5,000,000 before operation to 6,720,000 on eighth day showing some loss of water. Weight 4.9 kgr. Died during night. Autopsy at 10 A.M. in morning. Obstruction complete as tested by absence of bile in distal gut, although under pressure, water could be forced beyond the clamp. No peritonitis. Around the clamp in a mass of omentum there was a collection of dirty yellowish fluid. The intestinal wall showed some damage within the bite of the clamp (see microscopic examination). The stomach and proximal intestine were moderately dilated, and contained a small amount of bile and mucus. The mucous membrane of the whole tract appeared normal to gross examination, as did the kidneys and liver.

Microscopic Examination. The intestine within the clamp showed an advanced purulent peritonitis, destroying longitudinal muscular coat. Congestion of mucosa. Exfoliation of epithelium.

Kidney. Congested. Tubules filled with granular coagulum. Cells swollen and show marked granular degeneration in places approaching necrosis.

Liver. Section lost.

Pancreas. Marked congestion.

Bacteriology. Aërobic and anaërobic cultures from femoral blood, peritoneum, and liver showed no growth. A Gram positive coccus was obtained in pure culture from the abscess around the clamp in all tubes both aërobic and anaërobic. This was undoubtedly an infection passing through the gut wall where the clamp damaged it, since the same organism was isolated from the intestine.

No. 25. Dog. Weight 6 kgr. Fed twenty-seven hours before operation. Clamp applied 16 cm. below the pylorus. He took ether badly and made a poor recovery. He was not given the hypodermoclysis of normal saline solution. Condition seemed good the next day. Died that night. Autopsy not done until day following, about thirty hours post mortem. Obstruction complete under water pressure. No peritonitis. Stomach and proximal gut somewhat distended. Distal gut collapsed. Mucosa of stomach and proximal gut markedly congested. Liver, spleen, pancreas, and kidneys showed congestion.

Microscopic Examination. Stomach congested. Proximal intestinal mucosa shows intense congestion. Marked round-cell infiltration of tips of villi and exfoliation of cells.

Liver. Intense congestion. Considerable granular and fatty degeneration.

Kidney. Not examined.

No bacteriological examinations made because of delayed autopsy.

No. 26. Bitch. Weight 7.2 kgr. Exact duplicate in every way of No. 25, except that she received the saline injections daily, the first one of 150 c.c. being given at the close of the operation. She lived ten days, and showed the same symptoms as in other dogs described. There was a marked contrast to dog No. 25, which did not receive the saline. Killed with ether and autopsied immediately. Obstruction complete against a column of water 90 cm. high. No peritonitis. The stomach and proximal gut were dilated to about three times normal. The mucosa of stomach and proximal intestine were congested. The liver, kidneys, and spleen were congested.

Microscopic Examination. Proximal intestinal mucosa shows intense congestion and exfoliation of living cells.

Kidney. Shows congestion. Tubules contain coagulum and

occasional blood cells and show granular degeneration, in places very marked.

Liver shows intense congestion, atrophy of liver cords about distended capillaries and moderate granular degeneration.

Spleen shows much hypertrophy of the follicles.

Pancreas normal.

Cultures from femoral blood, liver, spleen, and peritoneum were taken. These were all without growth after four days, under both aërobic and anaërobic conditions, except one aërobic tube (four were taken) from the liver. This showed one colony of Gram positive cocci growing well to one side of the stroke of the loop.

No. 27. Bitch. Weight 11.5 kgr. Fed twenty-eight hours before operation. Clamp applied about 15 cm. below the pylorus. Lived twenty-four days with only moderate development of symptoms during first week. Then behaved like a normal dog. Re-operated upon on July 20. The clamp was not sufficiently tight to make a complete obstruction (compare with No. 22). It was tightened and the next day it had cut its way through the gut wall and the dog died of a peritonitis.

No. 28. Dog. Weight 6.5 kgr. Fed twenty-eight hours before operation. Clamp applied 11 cm. below pylorus. Post-operative course as in other cases. Died in fifty-six hours and body immediately placed on ice. Autopsy ten hours later. Obstruction complete. No peritonitis. Local infection around the clamp. Stomach and proximal intestine only slightly distended and contained a small amount of bile-stained fluid. The distal gut was totally empty. Two superficial ulcers were seen in the mucosa of proximal gut. The liver, kidneys, spleen, and pancreas appeared normal.

Microscopic Examination. Intestine not examined.

Kidney. Tubules swollen and show granular degeneration, very marked in places.

Liver. Intensely congested.

Bacteriology. Cultures from the femoral blood, the peritoneum, the liver, the spleen, and the local collection of fluid around the clamp all were without growth under aërobic and anaërobic conditions.

No. 29. Dog. Weight 8 kgr. Fed thirty hours before operation. Clamp applied 11.5 cm. below pylorus. Post-operative course same as in other cases. Received about one-fortieth of body weight of normal saline subcutaneously daily. He remained in excellent condition for eight days, during which time he lost a little over 2 kgr. in weight. He drank water each day which was always vomited. Pulse from 130 to 174. Temperature, 38.5° to 40° C. On the ninth day he was etherized and the abdomen opened. The obstruction was complete. The stomach and proximal intestine were much distended (Fig. 2), and filled with a greenish fluid of the thickness of pea soup. There was no peritonitis. The

splanchnic vessels were not much dilated, except those above the occlusion. The spleen was not enlarged. The liver and kidneys did not show much congestion. Sections were taken from the stomach, duodenum, distal intestine, liver, spleen, and kidney while the dog was still under ether, after which he was killed.

Microscopic Examination. The stomach is normal.

The proximal intestine shows marked congestion and an edema in the submucosa. The lesions here were not advanced, because the specimens were taken some hours before the animal would have died from the disease. The distal intestine is normal.

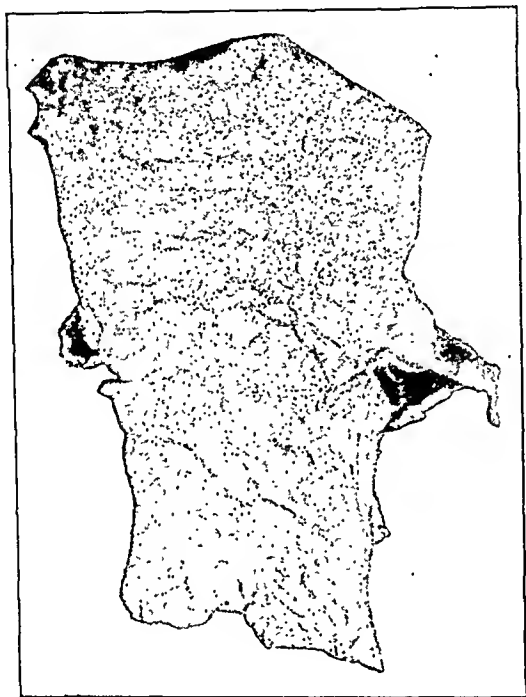


FIG. 2.—No. 29. Showing mucous surface of intestine at site of clamp. Note absence of damage to mucosa at this point and the congested appearance proximal to it. Also distention of duodenum above the clamp.

The liver is congested. The cells show granular degeneration and areas of necrosis are present.

The kidney is congested. Tubules contain granular coagula. The cells show granular degeneration.

The above series includes experiments on 11 animals which may be summarized. In 2 a complete obstruction was not obtained because the clamp was not sufficiently tight. These 2 animals were killed after twenty-one and twenty-four days respectively, while each was in good condition. They had emaciated a good deal, and one of them was weak, but otherwise they acted like normal dogs.

The remaining 9 dogs all showed a similar condition while living, and autopsy yielded the same findings in the organs. In some

dogs, particularly those which lived the longest, the dilatation of the stomach and the duodenum was very marked (Fig. 3, of No. 23).

Four dogs in this series were given sterile water by mouth only, and this they promptly vomited. They were, therefore, practically getting neither nourishment nor water, for if what they drank was not all vomited, very little absorption could take place from the stomach and duodenum. Beginning with the fourth dog, each dog

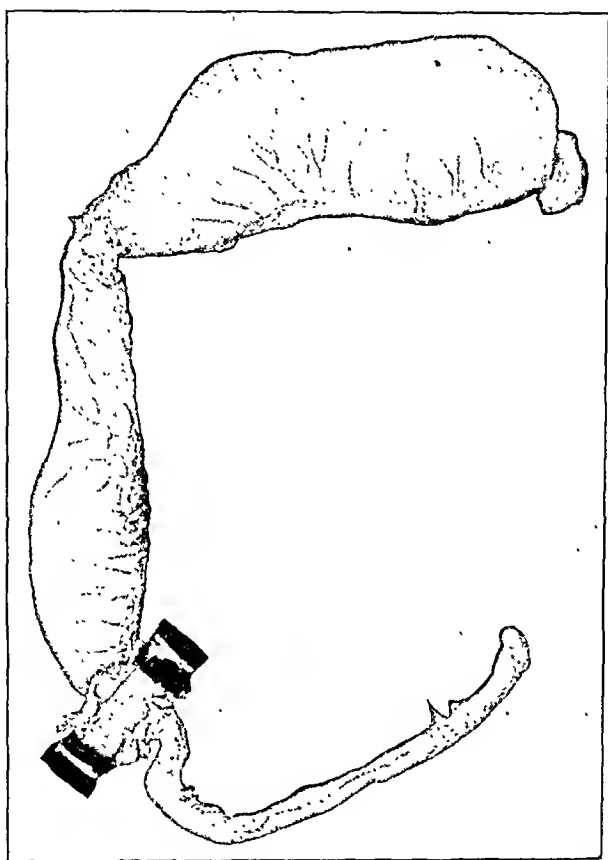


FIG. 3.—No. 23. Showing clamp in situ. Stomach and duodenum dilated. Vessels engorged.

received from 150 to 300 c.c. sterile normal saline solution, either subcutaneously, or by rectum, per day, and this was absorbed. In one case this was not given till the third day. This animal had then begun to act sick, but showed a marked improvement after the administration of the hypodermoclysis. In general, the dogs who received this saline, lived longer than the others. They sometimes drank sterile water in addition, but this they always vomited in a very short time. In many cases they refused to drink more than a few cubic centimeters. The 3 dogs which lived the longest

were all given the saline subcutaneously, and there seems no doubt that this procedure was very beneficial.

We attempted, by a count of red-blood cells, to determine whether the dogs not receiving it suffered from dehydration, with a consequent increase in the number of red cells per cm. There was not a sufficient variation from the normal, to throw any light on this point, the number ranging around 6,000,000 both before and after the saline injections. The saline may have acted in either of two ways. It may have prevented an actual dehydration of the tissues, which is a deleterious condition in itself, or it may have acted as a diuretic and thus aided the elimination of poisons by the kidneys. The longest post-operative life was ten days (2 dogs); a third dog lived just under nine days; the shortest period was thirty-six hours in a small fox terrier who never completely recovered from the operation. The average length of life was one hundred and thirty-nine hours in this series, as against sixty-seven hours in the series where the obstruction was produced by sectioning the intestine and inverting the ends, but it was only in the former that the aid of the saline injections was used.

It was, moreover, remarked that the second series in which no damage to the intestinal wall was produced was much nearer the normal throughout the experiment than was the first series in which the intestine was sectioned. So far as we know, no other experimenter has paid the same attention to producing an obstruction without any damage to the intestinal wall. There is evidence that the method is of advantage in excluding the complications which may arise from such damage. Clinically, we know that when a strangulation—however limited in extent—is superimposed on an obstruction, the course of the disease becomes much more acute. Medowoy,²¹ Koehler,²² and others, emphasize this point.

Murphy and Vincent²³ in their experiments, worked particularly on this phase of the question. In a simple obstruction in cats they found the intestinal wall very little damaged in four to six hours. When, however, the circulation was disturbed, particularly a venous stasis produced, a very severe change was present at this time. They conclude that "Interference with the circulation of the obstructed intestine is the vital factor in the production of the symptoms of ileus."

When the intestine is sectioned, and the proximal end sufficiently inverted to prevent the stomach and duodenal contents being forced through it, a local strangulation takes place. At autopsy there was always found in these cases a local damage to the intestinal wall at the inverted point, small in extent to be sure, but nevertheless sufficient to be the possible site of the absorption of

²¹ Deutsch. Zeitsch. f. Chir., cv, S. 1.

²² Mitteil. Grenz. d. Med. u. Chir., Band iv, Heft 2.

²³ Loc. cit.

a considerable amount of poison. Often, too, a very considerable intussusception of the invaginated stump was present. This mechanical damage, of course, is not an essential in producing death, because it was not present in the second series, and they died. We feel, however, that it has an important bearing on the problem, as we shall later, more fully explain.

We desire to call particular attention to the microscopic findings in these cases. The intestinal mucosa, proximal to the obstruction, shows a marked congestion. Marked round-celled infiltration is present, and exfoliation of the lining cells. Hemorrhages are often seen. There is present an acute hyperplasia of the lymph follicles. The submucosa is edematous. Distal to the clamp there is no change, or only a very slight change from the normal. The gastric mucosa shows only a congestion. The kidneys are markedly congested. The tubules contain granular coagula. The tubule cells are swollen and the seat of granular degeneration; not infrequently necrotic areas are seen.

The liver is congested and the cells show granular and fatty degeneration. Necrotic areas may be present.

The spleen shows marked congestion, and some hyperplasia of the lymph follicles.

The pancreas shows only congestion.

The above changes are those seen in many forms of toxemia, both bacterial and non-bacterial. They are found in the toxemia of starvation, of pregnancy, of delayed chloroform poisoning (Howland and Richards²⁴), and of many of the acute infectious diseases. They are, therefore, very strong evidence that in our dogs, some toxic substance was present in the circulating blood during life. The rapid emaciation, the progressive weakness and the high pulse rate, with a comparatively normal temperature, all support this evidence. The two cases, Nos. 22 and 27, in which the obstruction was not complete, indicate that the condition is not one of simple starvation, because these animals received no food and practically no water to drink (the saline was given subcutaneously as in the others) during a period of over three weeks, and yet remained in a condition of good health. They showed less emaciation and loss of strength during the experiment than did the fully obstructed dogs in one-third as long a period.

In order to test this point still farther, however, a dog was kept in the laboratory for two weeks, and received absolutely no food or water by mouth. The saline injections were given daily. Under this treatment he remained in an apparent condition of perfect health. He lost 29 per cent. of his body weight. There was no evidence of weakness. The pulse rate was from 70 to 120, and the temperature normal. A second dog had the clamp applied to the

²⁴ Jour. Exp. Med., 1909, ii, 344.

pylorus. He remained well (Fig. 4) for fifteen days, receiving only the subcutaneous saline injections. The toxemia of starvation is, therefore, not the determining factor in producing the symptoms or the pathological changes found in intestinal obstruction. We attempted, as mentioned above, to eliminate a bacterial origin, either direct or indirect, for the toxic substances, by withholding food from the dogs and allowing them only sterile water to drink, both before and after the operation, with the hope that we might produce a sterile condition of the stomach and duodenum above the occlusion. In this we were not successful, for in the 6 cases where a bacterial examination of the intestine above the clamp was made at autopsy an abundant growth of the usual intestinal flora was found. A

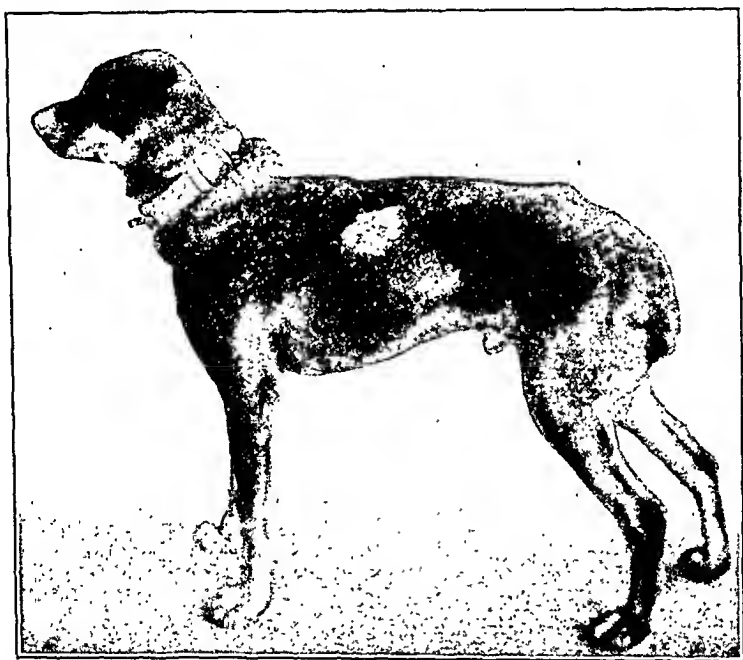


FIG. 4.—Dog with clamp on pylorus. Showing good condition after twelve days. Examination under ether on the fifteenth day, while the dog was still in good condition, showed the clamp to be tight.

further attempt to accomplish such sterilization was done in two cases (Nos. 30 and 31) by producing an intestinal fistula just distal to the duodenum (Fig. 1, c). We hoped by gastric and retrograde washing through this tract to get it clean and then obstruct it. Both dogs, however, died within a few days, and no further attempt in this direction was made.

We then turned our attention to an elimination of the bile, pancreatic, and duodenal secretions as a source of the poisons. To this end, in five dogs (Nos. 32 to 36) the following operation was done (Fig. 1, d). The pylorus was divided and the two cut ends closed by inversion. The intestine was divided just distal to the

duodenum, and the proximal end implanted in the jejunum about 30 cm. lower down. The distal end was implanted into the stomach. By this means the stomach emptied into the intestine just below the duodenum, and the bile, pancreatic, and duodenal secretions passed into the jejunum about 30 cm. distal to this. Our intention was to cause an obstruction with the clamp, just orally to the new duodenal outlet when the animals should have recovered from the anastomoses, thus having an obstruction of the stomach and about 30 cm. of intestine, but not of the duct-bearing portion of the tract.

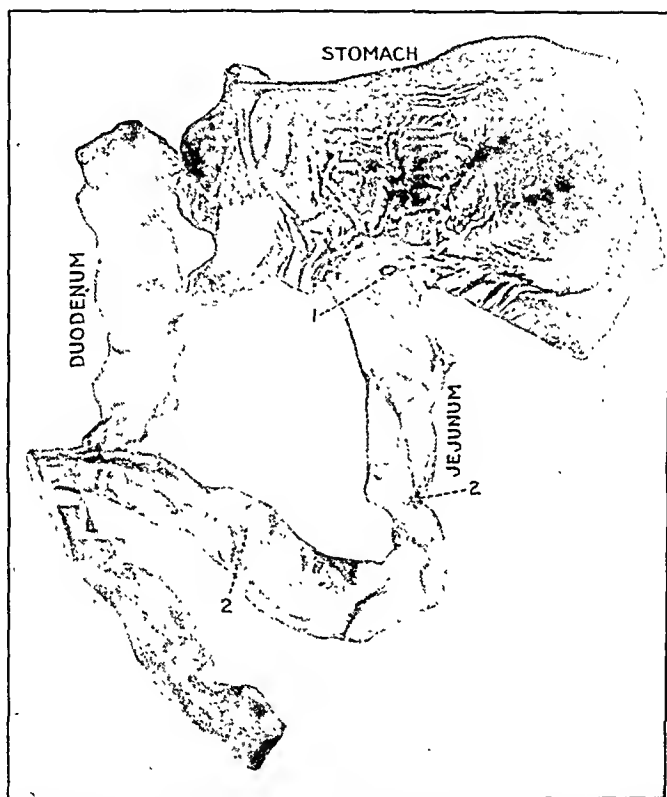


FIG. 5.—Showing damage to jejunum where the gastric juice passes into it without neutralization by entering duodenum; 1, perforation just below gastrojejunosomy; 2, ulcerations lower down.

For a few days following the operation these dogs did well, fully regained their appetites and seemed to be in good health. After about a week, however, they all began to act sick. They did not eat well, and sometimes vomited. They lost weight rapidly. Some of them developed diarrhea with bloody appearing stools. Four of them died in about four weeks with evidence of malnutrition. The autopsy showed, in two of these, that a very extensive damage to the intestine between the stomach and duodenal anastomosis was present. Ulcers were seen which were about to perforate (Fig. 5).

The stomach and this part of the gut contained partially digested blood.

The fifth dog seemed to be in fair condition after two weeks and on the nineteenth day the abdomen was opened under ether anesthesia. The anastomoses were satisfactory and no evidence of ulceration was present from the peritoneal surface. The occlusion clamp was applied just above the anastomosis of the duodenum with the jejunum. The following day the dog was in good condition; he had not vomited. He was given saline subcutaneously.

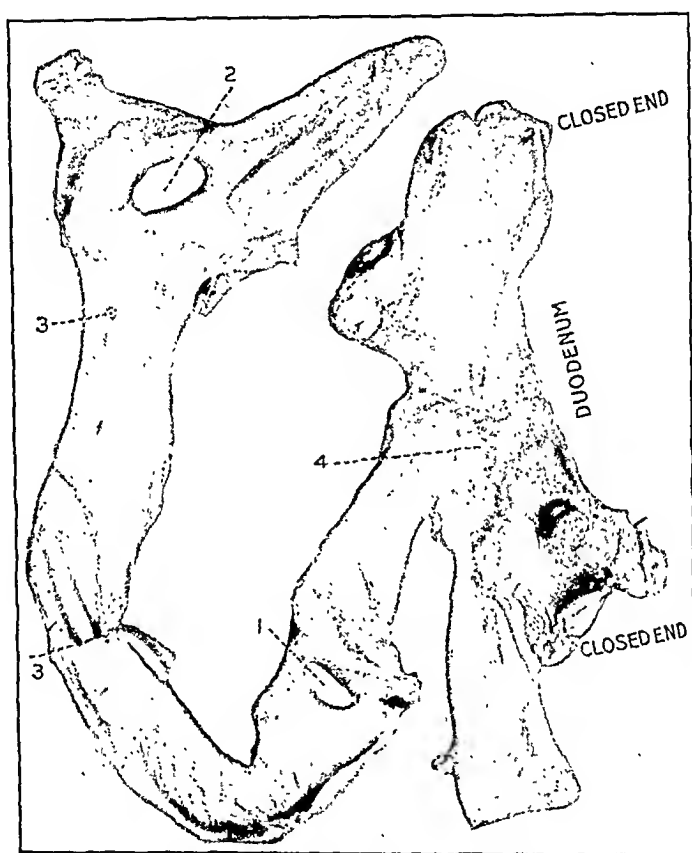


FIG. 6.—Showing perforation: 1, at site of clamp where it was applied nineteen days after anastomosis; 2, gastrojejunostomy stoma; 3, artefacts; 4, duodenojejunal anastomosis.

He died during that night and autopsy was done in the morning. The anastomoses were satisfactory. A general peritonitis was present from a perforation within the bite of the clamp (Fig. 6). The stomach and intestine anastomosed to it were distended with a dirty brownish fluid. On opening them the gastric mucosa was seen to be much congested; the mucosa of the jejunal segment was markedly congested and contained many hemorrhagic areas. The occlusion clamp had caused a perforation through one of these areas. The intestine below the duodenal anastomosis was entirely

normal in appearance. Similar ulcerations have been observed in the jejunum of dogs, after a long loop anastomosis to the stomach, by Exalto,²⁵ and many clinical cases of jejunal ulceration are reported following gastro-enterostomies.

Our attention was attracted by these cases to the damage done to the intestinal wall when the gastric juice unneutralized by the duodenal secretions comes into contact with the intestinal mucosa. Our effort to produce an obstruction in which the duodenal contents should not be stagnated had not been successful. But the symp-



FIG. 7.—Showing perforation (1) and ulceration (2) in doubly occluded stomach and duodenum.

toms developing in these dogs and the findings in the intestinal mucosa turned our attention in another direction which we think led to important results. In many ways these dogs behaved like the ones with an obstruction, the symptoms and the course of the disease being, however, much less acute. The microscopic examination of the intestinal mucosa, the kidneys and the liver showed, too, the same lesions as found in the simple obstruction. It, therefore, occurred to us that the damage we had noted in the mucosa, above the occlusion, might be a factor in the production of the

toxemia which caused the animal's death. To further test this point, the following experiment was done three times (Nos. 37 to 39).

The stomach was bisected and the two cut ends closed. A gastro-enterostomy was made between the eardiac half of the stomach and the first part of the jejunum. The occlusion clamp was then applied just proximal to this anastomosis, or the proximal end of the divided jejunum was implanted into the pyloric half of the stomach. In this way the secretions from the pyloric half of the stomach, the liver, the pancreas, and the duodenum were occluded within half of the stomach and the duodenum (Fig. 1, *e*). Two of these dogs died in approximately thirty-six hours; one in eighteen hours. They were very sick during this time. The pulse was 200 and over. They vomited. At autopsy the occluded portion was found enormously distended with a mixture of bile and mucus which was blood tinged. The stomach and intestinal wall were markedly stretched, the latter to paper thinness. In one case, at a point near the lower end of the duodenum, an ulcer was present which had perforated through the peritoneal coat, and around it was an area of necrosis 5 cm. in diameter. Proximal to this point were five extensive ulcers (Fig. 7). The mucosa throughout was markedly congested. In the other 2 cases no ulceration was seen, but the damage to the mucosa was very severe. In the jejunum, immediately below the gastric stoma, the mucosa was damaged in a similar way to that seen in the previous series, due to the unneutralized gastric juice entering it. Microscopical examination of the tissues gave the same findings as in the obstructed cases.

In the next series of experiments, Nos. 40 to 43, a loop of intestine below the duodenum was occluded by sectioning and closing the ends, or by the use of the clamps, and the patency of the tract reestablished by an anastomosis between the proximal and distal arms, above and below the clamps (Fig. 1, *f*). One was done high up in the jejunum, two in the middle of the small intestine, and one just above the cecum. The first of these dogs lived about eighty-four hours, and during the first three days of this time he seemed perfectly well. He drank water and took food without vomiting. He suddenly began to act sick on the fourth day and died that night. The closed ends of the loop were not tight, and leakage had taken place, resulting in peritonitis. The occluded loop showed an intense congestion and it was distended with dark bloody fluid. The mucosa showed hemorrhagic areas. The peritonitis, however, renders the case useless except for a study of the damage done to the occluded loop.

In the second case, leakage in a similar manner also took place, vitiating the result so far as the course of the disease is concerned. The occluded loop, however, was much distended with a thin

bloody fluid. The mucosa was markedly congested and at one point a superficial erosion was present.

The third dog, in which the occlusions were done with the clamps, lived about one hundred and ten hours. He remained well for three days, and then began to show marked symptoms similar to those seen late in the obstructed cases. Autopsy. The anastomosis was tight and the clamps had produced a complete closure. There was no abnormality seen in the alimentary tract, except in the occluded loop, which was 44 cm. in length and began 76 cm. below



FIG. 8.—Showing distended nearly gangrenous loop of intestine after double occlusion in upper jejunum. Rubber tubes indicating points at which clamps were placed; (1) entero-enterostomy. Mesenteric vessels perfectly patent.

the pylorus. This loop was enormously distended and contained about 500 c.c. of a bloody exudate containing granular material resembling hashed up blood clot. The loop was nearly gangrenous²⁶ throughout the whole extent of its convexity, the process being much more marked in the outer coats than in the mucosa (Fig. 8). No localized ulcerations were seen. The mesenteric vessels were filled with fluid blood, showing that gangrene did not result

²⁶ Cf. Roger and Garnier, *loc. cit.*

from their thrombosis. The gastric mucosa was not congested, but that of the duodenum was slightly so. The kidneys and liver showed a very marked congestion.

The fourth dog in this series had the clamps applied in the lower ileum, closing off a portion of the bowel about 25 cm. in length, proximal to the cecum, with an anastomosis between the proximal and distal arms. He was an old animal, nearly blind, and a poor operative subject. For three days he remained in fair condition. He drank water and did not vomit. The pulse was about 150 to 170 and the temperature 40° C. On the fourth day it was noted that the wound was badly infected, and he began to suffer from the dyspnea which is so often seen in old dogs. Ether was given and the abdomen reopened. The wound was badly infected, and a large intramural abscess was present. There was no peritonitis. The anastomosis had not leaked. The clamps were tight. The occluded loop was not distended. It contained only a few cubic centimeters of dirty brown mucus. The mucosa showed no evidence whatever of congestion. The condition was in marked contrast to that seen in the over-distended, ulcerated and gangrenous loops of the upper tract. The sickness of this dog we attribute to his age and general condition before operation, and to the severe infection in the wound, more than to the occlusion itself. McClure²⁷ and v. Baracz²⁸ have found similar results to this. They are to be explained by the absence of any irritative agents in the occluded lower ileum loop which cause damage to the mucosa. Hence, no poisons, bacterial or otherwise, are able to pass the defense of the lining cells and the animal remains unpoisoned (cf. occlusion of pylorus, page 388). The experiments of the last two series demonstrate that when, in a dog, any portion of the upper small intestine, either alone or with a part of the stomach, is occluded at both ends, and the patency of the alimentary tract reestablished by an anastomosis, the animal lives even a shorter time than in the simple high obstruction. He rapidly develops symptoms which come on only late in the obstructed dogs. The occluded loop is always markedly distended, and its wall is severely damaged by ulcerations or by destruction of the mucosa, and the damage may go on to gangrene. There is hemorrhage in the loop. If the loop receive the active digestive juices the damage is most marked in the mucosa; if it be lower down, the process is most marked in the outer coats. The vessels in the mesentery are not thrombosed, though an examination of the gut wall suggests this as a cause of the lesion. In the lower ileum the damage after four days may be very slight. If these lesions be compared to those already described as appearing in a simple high obstruction, they are seen to be of the same character, though much more severe. They resemble also the lesions

²⁷ Loc. cit.

²⁸ Loc. cit.

produced when the gastric juice unneutralized by the duodenal contents is emptied into the jejunum. From these findings it would seem that in all our experiments a destructive agent was at work which seriously affected the mucosa of the intestinal wall.

As is well known, one of the functions of the intestinal mucous membrane is to so alter the substances which pass through it into the blood, that they are not toxic to the organism. The changes which we have found in the structure of the mucosa, we believe, deprive this membrane to a greater or less extent of this function, and in consequence the toxic substances, which other workers have demonstrated to be present, actually enter the blood in their poisonous condition. If the damage to the mucosa is great as in double occlusion, the poisons enter the system rapidly, and the course of the disease is short. If the damage is less severe, as in simple obstruction, where oral drainage by vomiting can take place, the course of the disease is lengthened. Therefore, change in the intestinal mucosa, proximal to the obstruction, is to our minds, the key to the solution of the cause of death in intestinal obstruction. This change results from the irritating influence of the retained digestive juices, and the mechanical damage due to the stretching of the intestinal wall. It deprives the mucosa of its defence against the passage of substances which are poisonous to the organism. These poisons, therefore, slowly enter the blood, and work the damage seen in the kidneys and liver, and ultimately produce the death of the animal. The poisons are present in the normal stomach and intestine,²⁹ and it is not necessary to consider that the obstruction causes any alteration in them. Abnormal absorption is the essential factor.

This explains the total lack of symptoms observed in our dogs over a period of nearly a week in some cases. The changes in the mucosa of the intestine were not sufficiently great to deprive it of its defence against the passage of unaltered poisons (No. 23). When the change once developed, this abnormal absorption took place rapidly, and active symptoms ending in death soon resulted. The subcutaneous injection of saline was beneficial because it probably aided in the elimination of the poisons by the kidneys, as well as prevented a dehydration of the tissues from lack of water. Any method of producing the obstruction, which causes a mechanical damage to the intestinal wall, hastens the development of symptoms and death, because the defence is then locally broken down. We see in this an explanation of the much more severe type of the disease when a strangulation is superimposed on an obstruction.

In one dog the clamp was applied directly to the pylorus. This animal lived in a condition of good health for fifteen days (Fig. 4).

²⁹ Roger and Garnier, loc. cit.

During the first twelve days he received the saline injection subcutaneously and refused to drink any water. His condition remained so nearly normal that it was concluded that the clamp was not causing a complete obstruction. The saline injections were discontinued, and he was given water by mouth and 50 grams of chopped beef heart on the twelfth day and 75 grams on the thirteenth day. The next day he refused to eat anything more, but he drank water freely, some of which he vomited. On the fifteenth day he was etherized and the abdomen was opened. The clamp was found to have caused a complete obstruction. There was no peritonitis. The stomach was enormously dilated, filling nearly the whole abdomen. This dilatation had occurred only during the three days in which he received water by mouth, as determined by the measurement of his girth which increased from 30 cm., the normal size, to 50 cm. The contents of the stomach was water with remnants of finely digested meat. The mucosa was entirely normal in appearance. There was no congestion of any of the abdominal viscera. From this experiment it is evident that the gastric juice, when stagnated in the stomach itself, is not absorbed as a toxic substance, so long as the mucosa remains normal. As shown, however, in experiments 32 to 36, it produces changes in the small intestine, when unneutralized by the duodenal contents which permit the absorption of materials producing symptoms and pathological lesions in the organs analogous to those of an obstruction. These facts are very strong evidence that the damage to the mucosa occurring in ileus is a necessary factor in the production of the toxemia there seen.

The following is a summary of the findings of our work:

1. A high intestinal obstruction, that is, 10 to 30 cm. from the pylorus, in dogs, may not produce death for ten days, provided the gut wall is not damaged. If it is damaged by section and inversion the average life is only half as long.

2. There are found in the kidney and liver cellular changes which are the same as those found in many toxic diseases. The intestinal mucosa is found to be damaged to such an extent that it may readily be conceived that it has been deprived of its natural defence against the passage of toxic substances, unaltered, through it.

3. Bacterial invasion of the blood and organs does not necessarily occur.

4. Dogs deprived of food for forty-eight to seventy-two hours, may die as early as those fed ten to twenty hours before the obstruction is produced. Decomposition of foodstuffs is not, therefore, an essential element in causing death.

5. If a double occlusion of the alimentary tract, with reestablishment of the continuity of its lumen, above the lower ileum be produced, the damage to all the tissues is greater than with a simple

obstruction, and the course of the disease to a fatal termination is shorter. A double occlusion in the lower ileum produces much less damage than in the upper.

6. The action of the gastric juice, bile, pancreatic juice, and duodenal secretions are not a requisite in producing the symptoms and pathological changes seen in intestinal obstruction, because these are produced by a double occlusion in the upper ileum when none of these secretions are blocked.

7. Simple occlusion of the pylorus does not necessarily produce any evidence of a toxemia in two weeks, and the gastric mucosa at the end of this time shows no evidence of being damaged.

8. The above findings indicate that death from intestinal obstruction in dogs results from the presence of toxic substances in the circulating blood which produce fatal lesions in the kidney, liver, and other tissues. The essential factor which admits these substances into the blood is an injury to the lining cells of the intestine caused by the irritating action of the stagnated contents, together possibly, with the mechanical damage due to stretching. The poisons themselves may arise from the secretory activity of the various digestive glands, or from bacterial activity. They may be the same as those found in the normal tract or they may be substances newly formed under the conditions of stagnation. Whatever their source, they are innocuous so long as the mucosa remains normal.

We desire to acknowledge our indebtedness to Drs. Ewing, Lusk, Elser, and Huntoon of the Cornell Medical College, not only for valuable advice and suggestion in this work, but also for material aid in carrying out the pathological and bacteriological investigations connected with it.

LOSS OF EMOTIONAL MOVEMENT OF THE FACE WITH PRESERVATION OR SLIGHT IMPAIRMENT OF VOLUNTARY MOVEMENT IN PARTIAL PARALYSIS OF THE FACIAL NERVE.

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THE voluntary and emotional movements of the face are independent of one another, and one form may be lost without loss of the other. Von Bechterew¹ says a number of observations show

¹ Die Funktionen der Nervencentra, vol. ii, p. 1144 et seq.

positively that the emotional movements in man are accomplished by means of special tracts which have no relation to the tracts concerned with voluntary movement. Cases of paralysis are known in which voluntary movements of the face, or of the lower part of the face, were lost and emotional movements (laughing, crying) of the face were performed in a normal manner. In discussing these cases, Nothnagel remarked that when the voluntary movement of the face is lost in hemiplegia from a focal lesion, but both sides of the face take part in equal degree in emotional movement, one may assume that the optic thalamus and its connections with the cortex are uninjured. Cases in which the emotional movements of the face have been lost and the voluntary movements preserved have been reported by v. Bechterew, Nothnagel, Rosenbach, Kirilzew, Gowers, and many others.

According to v. Monakow,² it has long been known that in many cases of hemiplegia the face on the affected side cannot be moved voluntarily, but the paretic facial muscles at once contract, as well as those of the other side, when the patient laughs or cries. v. Monakow expresses his belief that a part of the sensory reflex tract for laughing or crying is situated in the optic thalamus.

The experimental work of Roussy³ throws doubt upon the optic thalamus as a reflex centre for emotional movements of the face, as does the work of Ernest Sachs,⁴ who, in the report of his experiments upon the optic thalamus states that stimulation produced facial movements of the opposite side. He adds: "It is desirable, perhaps, to repeat here that these motor phenomena constitute no evidence of special centres in the thalamus for automatic or rhythmic movements, as has been assumed by some authors." One possibly might make the objection that the results obtained in animals are not applicable to man.

Lewandowsky⁵ believes the opinion regarding the optic thalamus as an emotional centre is not well founded. There are so many negative cases in the literature that a relation of paralysis of emotional movement to thalamic lesions cannot be maintained. Even in the cases in which thalamic lesions have been found, different parts of the thalamus have been affected. It is not improbable, he adds, that the assumption of a relation between emotional facial movements and a thalamic lesion is without foundation.

The paralysis of one form of facial movement without impairment or with only slight impairment of the other may result from a lesion of the facial nerve, or may be a pseudoparalysis from imperfect innervation. I have observed persons who in smiling or speaking innervated one side of the face so much less than the other that paresis of one side seemed to be present, and yet the drawing up

² *Gehirnpathologie*, Nothnagel's System.

⁴ *Brain*, Part 126, vol. xxxii, p. 1909.

³ *La couche optique*, p. 185.

⁵ *Allgemeine Neurologie*, Part 2, p. 741 et seq.

of the corners of the mouth, as in showing the teeth, was equally good on the two sides.



FIG. 1.—In smiling, only the right side of the face showed contractions of muscles.



FIG. 2.—In showing the teeth, contractions of the muscles were only a little less pronounced on the left side of the face. The reproduction does not show these contractions so well as does the photograph. The photographs were taken after the operation. The dissociation of facial movements was more pronounced before the operation.

What I especially desire to call attention to at the present time is loss of emotional movement of one side of the face with preserva-

tion or possibly only slight impairment of voluntary movement of the same side, as indicative of a certain stage of peripheral facial palsy. I have observed this phenomenon especially in slight facial weakness resulting from the pressure of a tumor of the cerebello-pontile angle upon the facial nerve. The movement of the face normally is less intense in smiling or crying than in showing the teeth, and, therefore, a slight paresis of the facial nerve might cause loss of these emotional movements on one side of the face, and the weakness might be overcome by the forcible effort made to contract the lower part of the face in showing the teeth. The case was one referred to me by Dr. W. H. Snyder and Dr. Louis Miller, of Toledo, Ohio, October 23, 1910. In smiling the man drew up the right side of the face strongly and the left side weakly, but in showing the teeth or drawing up the corners of the mouth separately, the left facial weakness was slight. Dr. C. H. Frazier operated and found a tumor in the left cerebellopontile angle pressing upon the facial nerve.

It is important to recognize that this form of dissociation of facial movement may be the first sign of weakness of the facial nerve from pressure of a cerebellopontile angle tumor, and in connection with slight nerve deafness may be of localizing value. It is possible that the impairment of emotional movement may result, in part at least, from the pressure of the tumor upon the medulla oblongata and pons. I am unable to determine at present whether or not the impairment of emotional movement of the face occurs in most cases of tumor of the cerebellopontile angle.

THE RELATIONSHIP BETWEEN ERYTHEMA NODOSUM AND TUBERCULOSIS, WITH THE REPORT OF A CASE.

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ERYTHEMA nodosum has been variously regarded as a simple variety of erythema multiforme, as a definite specific contagious disease (Paulouch, Oppert, Batigne et al.), and as a secondary manifestation in many differing conditions, such as the infectious diseases, drug ingestion, alimentary disturbances, and nervous diseases.

Jouillié divided erythema nodosum into two classes—primary or so-called idiopathic and those secondary to infectious diseases, certain drugs and nervous disorders. In 1872 to 1878 Uffelman and Oehme reported some observations from which they concluded that tuberculosis was frequently a cause of erythema nodosum.

Cases reported by Schmitz, Comby, Oppert, Goldscheider, Buisine, Levy, Schamaun, Poncet, and others, have shown an association between erythema nodosum and tuberculosis. More recently Troisier and Chauffard, in France, and Otto Brian, in Germany have discussed the correlation of erythema nodosum and tuberculosis. Mlle. A. Pérel in her "Thèse pour le Doctorat en Médecine" discusses the relationship between erythema nodosum and tuberculosis, citing a number of cases from the literature and from her own experience, in which there was apparently a definite connection between the appearance of the erythema nodosum and a concomitant or subsequent tuberculosis.

Hildebrandt injected 5 c.c. of venous blood, taken from patients suffering from erythema nodosum, into the peritoneal cavity of guinea-pigs and succeeded in producing tuberculous lesions in them. Otto Brian repeated the experiment of Hildebrandt and was able, in one case, to infect 3 guinea-pigs with tuberculosis by injecting them with the venous blood taken from a patient with erythema nodosum. In all the other cases, however, in which this experiment was tried, he failed to infect a single animal. Chauffard and Troisier were able to produce an experimental erythema nodosum by the "intradermic injection" of tuberculin in very small doses and this experiment has been repeated successfully by several workers, notably Marfan, Carnot, Widai, and Benard.

A number of observers have maintained that in patients afflicted with such skin lesions as erythema multiforme, urticaria and the like, a reaction analogous to that obtained with tuberculin could be produced by the intradermic injection of diphtheria antitoxin, tetanus antitoxin and even with normal salt solution. Mlle. Pérel, together with Chauffard and Troisier, controlled their intradermic injections of tuberculin by the simultaneous injection of salt solution and the various sera, and in all but one case the control injection gave negative results.

Landouzy, in 1907, at the Congress of the French Association for the Advancement of Science, maintained that erythema nodosum was a local manifestation of a bacillary septicemia.

Chauffard and Troisier, in their intradermic experiments, were able to produce at the site of injection a nodule which, in all of its characteristics, appeared identical with the nodes in erythema nodosum. They believed that this experiment was evidence in favor of the theory that the plaques of erythema nodosum resulted from the conflict between the tubercle bacillus in the circulation and the antibodies which are present at certain points in the organism.

Otto Brian was able to demonstrate, by means of sedimentation with acetic acid and antiformin, in the venous blood of patients afflicted with erythema nodosum, an acid-fast bacillus, but excepting in one case he was not able to produce tuberculous lesions in guinea-pigs by injecting them with the blood in which these acid-fast bacilli occurred. He obtained positive reactions to the injection of tuberculin and to the von Pirquet skin test, but he did not think that this gave any proof that the erythema nodosum was as such of a tuberculous nature.

He concludes that: (1) The etiology of erythema nodosum is not uniform. (2) Tuberculosis is by no means the only cause of erythema nodosum; in fact, it is the cause apparently only in a small percentage of the cases. (3) The assumption that each case of erythema nodosum represents a rheumatic infection in special form is not well founded. (4) The throat is the portal of entry for the infection in many cases of erythema nodosum, but not for all.

Mlle. Péral in her thesis reports 22 cases in which a definite relationship existed between erythema nodosum and tuberculosis. Among these cases were several in which there was an apparent association between the erythema nodosum and tuberculous meningitis.

We offer the following report of a case of erythema nodosum which occurred as an early manifestation in tuberculous meningitis:

On January 24, 1910, there was admitted to the wards of the second medical division of Bellevue Hospital, a young Italian woman, aged twenty-five years. There was nothing in the family history nor in the past history which had any bearing on the present illness.

Two weeks before admission to the hospital she noticed an eruption on either cheek, occurring first as discrete papules and vesicles which shortly coalesced to form a continuous patch. The only subjective symptom at that time was the slight itching which accompanied the eruption. A few days later there appeared on the arms and on the legs numerous bright red spots and on the anterior aspect of the legs several hard, raised nodules, which were excessively tender on palpation. With the appearance of these nodules the patient complained of a general feeling of lassitude, anorexia, fever and pains in the joints, especially in the knees. The chief complaints on admission were the eruption on the face and limbs, fever, malaise, and arthritic pains.

The physical examination on admission showed a well-developed and well-nourished young woman, aged about twenty-five years, who did not appear to be very ill. The temperature was 100.5° , the pulse rate was 96, the respirations 24 per minute. The skin over the cheeks and to a lesser extent over the forehead was reddened,

thickened and sealing. The right pupil was slightly dilated, both pupils reacted promptly to light. The conjunctivæ were normal. The tongue was thickly coated. The throat was normal. The tonsils were not hypertrophied. The teeth were in good condition, there was no pyorrhea. The cervical glands were somewhat enlarged.

The chest was well developed. The heart and lungs were normal. No masses were made out in the abdomen. The liver, spleen, and kidneys were not palpable.

The skin over the chest, back, and abdomen was clear. Over the extensor surfaces of the forearms, and especially marked in the vicinity of the wrist joints on either side, there were noted a number of discrete macules, violaceous in color and irregular in outline, varying in size from that of a ten cent piece to that of a silver dollar. In some of these spots the color disappeared on pressure, while others were distinctly purpuric. Over the anterior aspect of the tibiæ and ankles an eruption similar to that described on the arms was seen and, in addition, over the thighs and legs and having no direct relation to the joints, there were noted several raised, red, sharply circumscribed nodules, varying in size and excessively tender on palpation.

The patellar reflexes were normal. There was no general glandular enlargement. Some tenderness was elicited by pressure over the lateral aspect of the knee-joints. There was no effusion into any of the joints.

The blood examination on admission showed: hemoglobin, 90 per cent.; white blood cells, 10,000; differential count: polymorphonuclears, 77 per cent.; lymphocytes, 17 per cent.; transitionals, 6 per cent.

The urine examination showed a specific gravity of 1034, no albumin, no sugar, no indican. On microscopic examination a few epithelial cells, a few white blood cells, and very rarely a hyaline cast were found.

The case then presented on admission: An erythema multiforme on the face and on the extremities accompanied by an erythema nodosum.

During the first three weeks of the patient's stay in the hospital there was no change in the condition. The temperature varied between 99° and 103° F. The eruption on the face gradually cleared up. During this time several crops of nodes appeared.

On February 18, twenty-five days after admission, the patient said that she felt well and that she desired to leave the hospital. No new nodes had appeared for several days. There was no longer any pain in the joints. The erythema had entirely disappeared and the purpuric eruption on the arms and legs was fading rapidly. Her malaise and anorexia had entirely disappeared, and her appetite was good. One symptom alone remained unchanged, namely,

the fever, which continued to run a remittent course, varying between 99° and 101° F. A blood culture made on February 24 was negative. On February 26 the patient complained of pain in the epigastrium. This was followed by persistent nausea and vomiting. She became drowsy and apathetic, taking no interest in her surroundings. An ophthalmoscopic examination at this time showed a perfectly normal fundus; there was no choking of the disks.

For the next week the nausea and vomiting continued, there was a total inability to retain food. The patient lost in weight rapidly. The temperature continued to be remittent in type. The pulse was rapid, irregular, and of low tension.

On March 2 the patient developed a slight cough, and on examination of the lungs at this time there was discovered over the base of the right lung behind, dulness on percussion, prolonged and high-pitched expiration, bronchial voice, and many medium moist rales.

A blood count done at this time showed: hemoglobin, 60 per cent.; white blood cells, 13,000; differential: polymorphonuclears, 74 per cent.; large mononuclears, 14 per cent.; lymphocytes, 11 per cent.; transitionals, 1 per cent. A spinal puncture was performed and 7 c.c. of slightly turbid fluid under moderate pressure were withdrawn. The report from the laboratory was that the fluid was "negative for tubercle bacilli." A cyto-count was unfortunately not made.

There was now a marked change in the patient's condition. She had become extremely restless; there was an almost continuous cephalic cry; the head was retracted and the neck was rigid. The pupils were dilated and irregular. A convergent strabismus was present. The ophthalmoscopic examination revealed a double choked disk. No tubercles of the choroid were observed. The face was somewhat flattened on the right side, the mouth was drawn to the left and the tongue deviated sharply to the right. A well-marked *tache cerebrale* was present. A marked Kernig's sign was elicited. The patellar reflex on the left side was absent and diminished on the right side. The respirations had assumed the Cheyne-Stokes type. The pulse was rapid, weak, and irregular. On lumbar puncture 44 c.c. of clear fluid were obtained under considerable pressure and the presence of tubercle bacilli was demonstrated in this fluid. The patient died on March 10.

The autopsy findings were as follows: Tuberculous lymphadenitis of the cervical and mediastinal glands. Tuberculous bronchitis and bronchopneumonia involving the right lower lobe. Localized miliary tuberculosis of the right lung. Tuberculous meningitis. Brown atrophy of the heart. Parenchymatous degeneration of the kidneys. Otitis media involving the right ear.

ON CERTAIN CHANGES IN THE ELASTIC TISSUE OF THE PELVIS OF THE KIDNEY, AND THEIR RELATION TO HYDRONEPHROSIS.

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INDUCEMENT to this study was given by a frequent occurrence of a dilated pelvis of the kidney, which assumed at times extreme dimensions in cases of arteriosclerotic and senile kidneys, and in advanced productive nephritis. No extrarenal obstruction or anomalies of insertion or angle of the ureter could be discovered.¹

In some of these cases the kidneys presented the picture of a long-standing, double hydronephrosis, although the extent of the lesion was at times different on both sides. In a number, particularly the aged, the lesion had become associated with an inflammatory condition of the pelvis, but only in a few it assumed a purulent character.

These observations extended over 505 autopsies performed during the year 1909. Among them were 15 which showed a marked dilatation of the pelvis of the kidney; in 3 this was complicated by a purulent pyelitis. In none was any common obstruction or abnormality in the relationship of the ureter to the pelvis discovered, which would account for retention of urine. The ureter was not dilated in these cases, but the walls of the pelvis of the kidney were considerably thickened. The urethra was found intact, and the walls of the bladder were not affected. In several cases the disease was not the same on both sides, and in some early instances parts of the kidney were still intact, while in others considerable flattening of papillæ had taken place with much distention of the calices. Below are cited the extreme cases:

CASE I.—An emaciated man, aged seventy years, had died from lobar pneumonia of the upper and middle lobes of the right lung and pneumococcal meningitis. The heart (510 grams) was considerably hypertrophied, particularly the wall of the left ventricle. Urinary bladder and urethra presented no special change. The renal arteries were both somewhat atheromatous. The renal cortex was fairly well preserved. The right kidney (112 grams) was somewhat reduced in size, its capsule slightly adherent and thickened, its cortex irregularly reduced, and its vascular markings irregular as in the usual forms of arteriosclerotic atrophy of the kidney. The pelvis of this kidney was considerably distended

¹ An illustration of this disease will be found in my monograph, *The Anatomic Histological Processes of Bright's Disease*, Philadelphia, 1910, Fig. 45.

and its walls thickened. The left kidney was virtually transformed into a sac. Its pelvis was enormously distended and the kidney substance almost completely lost. Microscopically, what kidney tissue had remained showed the glomeruli almost completely overgrown with fibrous tissue, and the tubules obliterated. In some remaining tubules the lumen had become largely distended and their lining cells transformed into flattened epithelium.

CASE II.—An emaciated woman, aged eighty-eight years, had been under observation for progressive weakness and mental enfeeblement for six months. Her urine had been increased in amount and always presented a small amount of albumin and casts. Toward her end she became edematous and died of cardiac failure. Autopsy showed a heart of 300 grams, atrophic. There existed general arteriosclerosis. Both kidneys were considerably reduced in size (150 grams); the pelvis in both was markedly dilated and its walls slightly thickened. The urinary bladder was somewhat dilated and its walls thin and atrophic. There was no suppurative condition in any-part of the urinary tract.

CASE III.—The third case presented much the same appearances, but had a superadded pyelitis. It occurred in a wasted male, aged sixty-nine years, who for one year had been progressively wasting, and had been recognized to have nephritis. There was a slight increase in the amount of urine with some albumin and casts, but never any pus. He died of gradual cardiac insufficiency. At autopsy the heart (300 grams) was atrophic, and there was a considerable degree of arteriosclerosis. The right kidney (150 grams) showed a moderate degree of arteriosclerotic atrophy, and the left (75 grams) was much reduced in size, while on section its pelvis was markedly dilated, and the calyces were so distended as to almost completely obliterate the kidney tissue. The pelvis was filled with a thick cheesy pus. Microscopically, no organisms were found, but the lesion was certainly not tuberculous. The ureters were patent and the urinary bladder was not hypertrophied nor did it contain any purulent material. There was a history of gonorrhea twenty years previously, but no apparent trace of this was determined at autopsy.

We deal, therefore, in this series with cases of hydronephrosis of all grades, from dilated calices to an almost complete obliteration of kidney substance and the formation of a large sac; some complicated by pyelitis; in all the direct cause of the lesion was obscure.

In a recent very extensive experimental and anatomical study of this disease, Ponfick² classifies it into two great groups, one with manifest, the other with obscure or doubtful etiology. Of a total number of 76 cases studied, 53 had a manifest cause, while as many

² Beiträge zur pathologischen Anatomie begründet von Ziegler, Band xv, Heft 1.

as 26 belonged to the latter and most interesting class. It is frequently asserted that hydronephrosis of obscure origin finds an explanation in a valve-like reduplication of a fold of mucous membrane at the junction of ureter with kidney pelvis. Ponfick, however, attributes such changes in the mucous membrane in infantile and in a certain number of cases of adult hydronephrosis to urinary concretions, which, having become lodged at the orifice of the ureter, produce urine stasis, and by irritative processes give rise later to the formation of an obstructing fold of mucous membrane, which persists even after disappearance of the concretion. In Ponfick's opinion the condition is, therefore, acquired and not developmental. There still remain, however, cases of obscure hydronephrosis without any such fold formation. Ponfick believes these due to an abnormal course of the ureter, producing an abnormal degree in the angle which the ureter forms with the pelvis of the kidney. Incidentally Ponfick mentions that the progress of the lesion may be aided by a gradual atrophy of the contractile elements which accompany the induration of the intermuscular connective-tissue bands of the pelvis. It does not appear that he attributes to these anatomical changes in the pelvis any essential role for the production of the hydronephrotic process.

The explanations of Ponfick are not applicable to the cases under consideration. In none of them were there evidences of previous concretions with changes in the mucous membrane or an abnormal angle or course of the ureter. Moreover, the irregularity in the development, as exemplified by early cases, its constant occurrence in diseases associated with slowly progressing atrophy of renal substance, and in the aged, suggested that pathological changes in the contractile elements might be of greater consequence than usually supposed. For the study of the changes in these structures the kidneys of about 100 cases of various kinds were sectioned.

The normal mucous membrane of the pelvis of the kidney contains a considerable amount of elastic tissue, which is regularly distributed in delicate fibers between the connective tissue of the mucosa, submucosa, and the muscle bundles. Elastic fibers enter, therefore, abundantly and widely into the structure of this mucous membrane. It has been found that this elastic tissue shows marked and important changes in various diseases of the kidney.

In the type of cases related above, that is, in the senile, arteriosclerotic kidney and in productive nephritis, in so far as they are uncomplicated by any diffuse inflammation of the pelvis of the kidney, the elastic tissue had become very prominent and was apparently much increased, while the connective tissue and muscular elements were atrophic and in extreme cases lost. Thus, in certain cases the elastic elements made up almost the entire bulk of the pelvic tissue. These differed, however, very markedly

from the delicate, evenly distributed fine fibers found in the normal mucous membrane. They were coarse, in places very thick and hyaline, fibrillated, frequently broken and disintegrated. The increase of elastic elements seems to be particularly marked near places where loss or fibrous contraction of kidney substance has occurred; for instance, immediately adjoining the flattened papillary portions of the kidney substance. The pictures thus obtained remind one very much of the changes occurring in arteriosclerotic arteries.

In all cases of pyelitis, whether from direct obstruction or implanted on a preëxisting hydronephrosis, or complicating a productive nephritis, the elastic tissue is destroyed, in purulent cases very rapidly, and eventually disappears entirely. This change is analogous to the behavior of elastic tissue in other inflamed organs. Non-purulent pyelitis, particularly near the papillary portion in close proximity to the kidney substance, is frequent in productive nephritis. It is difficult to determine its exact relation to the nephritic process, but it has a destructive influence on the elastic tissues of the pelvis. In this event there occurs also a gradual dilatation of calices and kidney pelvis. When this inflammatory process is localized it may be followed by elastic thickening of neighboring parts.

In a case of obstructive hydronephrosis, complicated by a pyelitis due to a cancer of the uterus, there occurred complete loss of elastic tissue. It would be interesting to investigate more thoroughly in the future the behavior of the elastic tissue in uncomplicated obstructive hydronephrosis, as well as the fate of the elastic tissue in specific inflammations of the pelvis of the kidney.

It would appear that the increase in elastic elements in the form of coarse lamellæ is probably a compensatory change incident to primary weakening and disintegration of these structures, together with progressing atrophy of the other component parts of the kidney pelvis. As in the case of arteriosclerotic arteries, it never appears to succeed in fully establishing reparation, but is prone to undergo disintegration. Thus a progressive weakening of these structures occurs, which in association with the atrophy of the fibrous and muscular parts leads to dilatation of the pelvis and stagnation of urine and true hydronephrosis.

It is not easy to determine exactly how far inflammatory conditions within the kidney parenchyma contribute toward these events. They may aid by a reduction of kidney substance, or a co-existing localized inflammatory extension within the pelvis of the kidney may be the factor. In such cases compensatory elastic thickening follows. But it has not been possible to demonstrate the formation of new elastic fibers after they have once been extensively destroyed by a general purulent pyelitis.

It does not seem that an increased urine output is of essential

consequence, as other diseases with marked polyuria, but without changes in the elastic tissue of the kidney pelvis, apparently do not lead to hydronephrosis.

Practically it remains important that an idiopathic hydronephrosis, which at times is conspicuously associated with inflammatory changes or even purulent pyelitis, is apt to occur in elderly people, and in those with contracted kidneys.

THROMBO-ANGIITIS OBLITERANS: A CLINICAL AND PATHOLOGICAL STUDY.

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PRESENILE spontaneous gangrene,¹ or so-called juvenile gangrene, at one time belonged to that ill-defined group of symptom complexes known as the vasomotor trophoneuroses. This group was made to embrace allied or intermediate conditions, including simple acrocyanosis² erythromelia, acroparesthesia³ erythromelalgia,⁴ and Raynaud's disease.⁵

From Raynaud, Mitchell, von Winiwarter, Munro, Cassirer, Strauss,⁶ and, finally, Buerger, we have had various contributions on the clinical and pathological aspects of one or more of the above-named conditions. An analysis of the clinical signs and symptoms of any one of these conditions will show that they manifest themselves by a combination of one or all of three main symptom groups—vasomotor, sensory, and trophic.⁷ The vasomotor include hyperemia, syncope, asphyxia; the sensory, pain, hyperesthesia, and paresthesia; the trophic, ulceration, gangrene, and dystrophies of the skin. Acrocyanosis, the simplest type, represents one symptom from the vasomotor group. Erythromelalgia includes hyperemia from the vasomotor group, and pain from the sensory. Raynaud's disease embraces all three groups; of these the vasomotor are hyperemia, syncope, and asphyxia;

¹ Leo Buerger, *Thrombo-angiitis Obliterans*, *AMER. JOUR. MED. SCI.*, 1908, cxxxvi, 567.

² Cassirer, *Die Vasomotorisch tropischen Neurose*, S. Karger, Berlin, 1910.

³ Schultze, *Ueber Akroparesthesie*, *Deutsch. Zeitsch. f. Nervenh.*, 1892, iii, 300.

⁴ S. Weir Mitchell, *Phila. Med. Times*, November 23, 1872.

⁵ M. Raynaud, *Thèse de Paris*, 1862.

⁶ *Arch. f. Psychiat.*, 1905, xxxix, 109.

⁷ Barker and Sladen, *Jour. Nerv. and Ment. Dis.*, December, 1907.

the sensory, pain, anesthesia, and paresthesia; the trophic, gangrene.⁸

Unfortunately, the pathological interpretation of these affections has not been clearly elaborated. Clinical classification, however, has advanced more rapidly and we have now numerous, nearly allied clinical conditions, satisfactorily classified, but without adequate pathological explanation. In the attempt to offer a pathological explanation for presenile spontaneous gangrene, von Winiwarter, in 1879, claimed that the terminal gangrene in many of these cases was the result of an occlusion of the lumen of the vessels by means of an obliterating endarteritis, which consisted in proliferation of the fibrous and cellular elements of the intima—endarteritis obliterans. Weiss and von Monteuffel,⁹ subsequent to von Winiwarter, claimed that the disease is caused by a primary endarteritis, with the formation of a white descending thrombus, with subsequent organization and arteritis.

That *senile* gangrene is due, in most cases, to endarteritis obliterans is not questioned, but Buerger,¹⁰ in 1908, advanced a new view, maintaining that *presenile* spontaneous gangrene was not a protean manifestation of an arteriosclerotic process, but an altogether new pathological entity, depending upon the primary formation of *obturating thrombi* in the arteries and veins, and to which he gave the name thrombo-angiitis obliterans.¹¹ He showed that the red thrombus is the precursor of the condition; that the process does *not* extend from above but from below upward; and that the lesion may occur in vessels devoid of endarteritis.

According to Buerger,¹² presenile spontaneous gangrene is a distinct clinical and pathological entity, characterized by thrombotic occlusion of arteries alone, or of arteries and veins, giving subjective manifestations, chief among which are pain and the peculiar symptom of intermittent claudication, and presenting objective phenomena, the most important of which are redness in the dependent position of the limb (erythromelia), marked blanching in the elevated position, evidence of arterial occlusion in the form of pulseless vessels (popliteal, anterior and posterior tibial, dorsalis pedis, etc.), trophic disturbances of moderate extent and of even grave consequence, often terminating in gangrene of one or both lower extremities. Clinically, thrombo-angiitis obliterans may show many variations from a set form, and this accounts for the fact that the true condition is so frequently over-

⁸ Barker and Sladen, *loc. cit.*

⁹ Cited by Buerger and Brooks, *Jour. Med. Research*, September, 1911, vol. xxv, No. 247.

¹⁰ *Loc. cit.*

¹¹ Quite recently Ch. Baumler describes this condition under the caption *Arteritis Thrombotica*, v. Benzoldt and Stintzing, *Med. and Therapic.* (Personal communication from Dr. Buerger.)

¹² *AMER. JOUR. MED. SCI.*, January, 1910.

looked. Brooks¹³ thinks that the vascular changes alone do not explain all the manifestations, but that the condition is also trophic in origin, and his histological studies showed distinct interstitial and parenchymatous neuritis and atrophic changes in the voluntary muscles, apparently secondary to the neuritis.

The gross process may be said to embrace distinct morbid processes. (1) An obliteration of the lumen of the large arteries and veins by means of an obturating thrombus, which later becomes vascularized and organized by growing in of "capillary buds" from the media and adventitia with subsequent canalization of the thrombotic tissue. (2) A periarteritis and periphlebitis, with a marked agglutinative process, due to fibrous tissue proliferation in and about the adventitia, and which binds arteries, veins, and nerves together into one conglomerate cord. In some cases, the agglutination is so dense and firm as to render dissection into the component elements almost impossible. (3) An associated or coincidental arteriosclerosis of varying degree.

In a typical case (quoted from Buerger)¹⁴ "the vessel is seen to be filled with a grayish or yellowish mass that can be distinctly differentiated from the annular wall of the vessel, and that appears to be pierced at one point (more rarely at a number of points) by an extremely fine opening through which a minute drop of blood can be squeezed. Such obturating tissue is firm in consistency and does not at all resemble the crescentic or semilunar occluding masses typical of arteriosclerosis. The vessel itself is usually contracted, so that its wall appears somewhat thickened." The vessels most often affected are those of medium caliber—the small distal arterioles are rarely if ever involved, and the tendency is for the thrombosis to extend up the leg rather than down. If a sufficient number of sections are made, the process may be followed from the fresh, red, recent thrombus, with a cone-shaped extremity, projecting into the lumen of an apparently normal vessel, to the old gray, yellow organized clot. Some arteries may be entirely free from the disease (in our case the peroneal artery was absolutely intact), while other vessels (anterior tibial, posterior tibial, dorsalis pedis, etc.) may show morbid changes of varying degrees of intensity. Buerger, therefore, concludes that the apparently normal condition of the vessel above and below the occluding masses, and the transition into the thrombosed areas speak for a thrombo-angiitis and thrombophlebitis instead of a proliferative obliterative process from the intima of the arteries and veins.

Histological examinations of the stained sections show a considerable amount of organized blood clot, occluding the lumen and often associated with certain characteristic changes in the media. The whole picture gives the impression of an extensive

¹³ Jour. Med. Research, September, 1911, vol. xxv, No. 247.

¹⁴ Loc. cit.

intimal and subintimal proliferation, hence the original designation endarteritis obliterans. Further study, according to Buerger, by means of special elastic tissue stains, shows that there is no intimal hyperplasia, but that the new tissue arises from organization at the periphery of an obliterating thrombus; in arteriosclerosis there is a large amount of elastic tissue parallel to the internal elastic tissue membrane and extending into and being incorporated with the characteristic sclerotic plaques. In the process under discussion, there is no noteworthy increase in elastic tissue, and such newly formed tissue as is observed can readily be seen to arise by organization at the periphery of a thrombus.

Thrombo-angiitis obliterans usually manifests itself by well-defined clinical signs and symptoms. The course of the disease, however, is variable, but is well illustrated by the following case:¹⁵

S. K. (Case No. 15,241), male, aged forty-nine years; a Hebrew, born in Poland; has lived in New York City for the last thirty years, during the last seventeen of which he has been employed as a street cleaner. The patient entered the hospital on November 18, 1910, complaining of "pain in the feet." Interesting features in the family history are fatal diabetes mellitus in an uncle and a cousin. The patient states that he has enjoyed excellent health up to the present illness. Venereal infection is denied and there is nothing in his personal history to suggest a syphilitic infection. For the last twenty years the patient has indulged in beer and whisky rather freely. For fifteen years he was in the habit of drinking three or four glasses of whisky daily, and for the last three years has been a considerable user of beer. Throughout his life the patient has smoked considerably, averaging twenty cigarettes per day. About two years ago he became impotent, which condition has persisted up to the date of his admission to the hospital.

The present illness began eight months ago, when the patient commenced to experience a "cold feeling" or a sense of numbness in the toes of the right foot in cold weather. This numbness was always associated with low temperatures and was not induced by inclemency of the weather. Occasionally, the left foot would be similarly affected, while at other times, both feet would be affected simultaneously. This feeling of numbness would come on about eight o'clock in the morning; the toes would appear blanched and were "apparently dead." After rubbing the toes or walking for a few minutes, the blanched, cadaveric appearance would be replaced by a dark red suffusion, quickly becoming livid or cyanotic. There were sporadic attacks of pain—cramp-like in character—in the calf of the leg, which would interfere,

¹⁵ We are indebted to Professor Edward Quintard for the privilege of reporting this case, from the medical wards of the New York Post-Graduate Medical School and Hospital.

temporarily, with locomotion. This condition, of alternating ischemia and erythromelia, persisted, with slight if any change, for about three months, when the patient began to experience "indefinite pains" in the sole of the right foot, associated with "drawing sensations" along the upper and inner part of the leg. Elevation of the leg from the pendant position to beyond the horizontal would elicit excruciating pain, while the toes would become extremely pale and bloodless. A short time after the onset of the above pain, the patient became "short of breath" upon exertion. For his dyspnea he visited various dispensaries and was treated for "heart disease" for a number of weeks, with a resulting gain in weight and strength.

The above symptoms persisted unabated up to three weeks before his admission, when the pain became very greatly exaggerated and was compared with the "sticking of pins" in the toes, or like "blowing steam over the foot," and was so severe as to prevent walking. Coincidentally, an eczematous rash appeared over the arms, legs, and abdomen, characterized by an intense pruritus.

Physical Examination: Temperature, 98.6°; respiration, 16; pulse, 100; weight, 122 pounds. The patient is a fairly well-nourished man, aged about fifty years, and does not look ill. The skin shows a diffuse, scaly, red, maculopapular eruption, with numerous scratch marks, suggesting eczema. There are many dilated venules over the cheeks and nose. The lips, ears, and finger tips are slightly cyanotic. The pupils are round, equal, and react to light and accommodation. A well-marked venous pulsation is to be seen in both external jugulars. The superficial glands show a moderate degree of adenopathy. Examination of the lungs reveals a moderate emphysema with slight relative dullness over the right apex. Expiration is prolonged, of low pitch, and accompanied by "wheezing rales." The heart is normal in size and outline; there are no murmurs or thrills. The first sound, at the apex, is somewhat rough, while the second sound, at the base, is only slightly accentuated. The blood pressure determination shows systolic, 120 mg. of Hg; diastolic, 75 mg. of Hg. The abdomen, spine, rectum, and external genitalia are negative. The reflexes are somewhat sluggish, but react equally. All the toes of the right foot and to a lesser extent the left foot are markedly livid when held in the pendant position. In the horizontal position the color is lessened to a pink, which spreads over the dorsum and sole of the foot. At an elevation of 15 degrees, "the angle of circulatory sufficiency," the foot becomes normal in appearance, while at 35 degrees of elevation the foot becomes markedly ischemic with the simultaneous development of excruciating pain. There are no blebs or ulcerated areas. The femoral artery pulsates, but no pulsation can be determined in the popliteal, dorsalis pedis, or posterior tibial arteries. The toes are extremely

sensitive to pressure; movement causes great pain. Along the inner and upper portion of the tibia are a few irregular, tender nodosities, not attached to the overlying skin and apparently belonging to the internal saphenous vein.

Blood examination: Hemoglobin, 70 per cent.; erythrocytes, 3,500,000; leukocytes, 10,000. Differential count: Polynuclears, 71 per cent.; large lymphocytes, 10 per cent.; small lymphocytes, 19 per cent.; eosinophiles, 4 per cent. Repeated complement fixation tests, both by the Wassermann and Noguchi methods, were negative. The coagulation time was normal, with the Russell-Brodie apparatus.

X-ray examination of both extremities showed no bony abnormalities.

Urinalysis. The average daily excretion amounted to about 800 c.c. The urine was acid, of specific gravity, 1025; showed no albumin and no sugar. Microscopically, there were found a few hyaline casts, a few disintegrated pus cells, no erythrocytes and no crystalline matter.

Subsequent course: From the time of admittance on November 18, 1910, until December 6, nineteen days in all, the patient presented no distinct signs of any trophic disturbance. On December 7 there appeared upon the under surface of the second toe of the right foot a small purple area, surrounded by a zone of inflammation, which marked the beginning of a definite gangrenous process. Within a few days the entire distal phalanx progressed to complete gangrene. Coincidentally, a small gangrenous area appeared along the outer border of the little toe of the same foot. This latter process was very slight and quickly subsided. However, on December 23, the two distal phalanges of the second toe were completely gangrenous with a moist, ill-defined line of demarcation. Within the succeeding month, contact ulcers began to appear on the adjacent borders of the first and second toes at the points of apposition with the gangrenous second toe. On February 9, or eighty-three days from the time of admittance, areas of gangrene began to appear over all the remaining toes. A large hemorrhagic bleb extended from the base of the toes, well up over the dorsum of the foot and passed gradually into a miliary, vesicopustular eruption with marked intervening lividity. During this time there were no changes taking place in the left foot.

Treatment consisted of hot air baths twice a day, to both legs, at a temperature of 140° to 180° F., with local applications of the official belladonna ointment, and codeine in grain doses, when necessary, for pain. There was some relief of pain, but the gangrenous process progressed. Amputation was recommended and readily assented to by the patient. On February 13, 1911, the right leg was amputated above the knee by Dr. Samuel Lloyd. The wound healed by primary union and the patient was discharged on March 3, 1911, apparently well.

Pathological Report. A very careful anatomical dissection of the vessels of the amputated limb showed extensive thrombotic involvement of all the large arteries and veins. In the popliteal artery the process commenced at about the upper level of the condyles of the femur, and from this point to the bifurcation there was a typical thrombotic occlusion of the lumen of the vessel. At the proximal end was found a recent, bright, red thrombus with conical extremity which passed gradually into a yellow material not unlike bone marrow, but of firmer consistency. In a few places the continuity of the occluding thrombus was interrupted by the appearance of clear spaces, bounded by apparently normal intimal walls. Near the point of bifurcation the material was gray and showed the beginning of canalization of the thrombus by two pin-point channels, through which minute drops of blood could be squeezed. The anterior and posterior tibial arteries showed similar thrombotic changes, in varying degrees of intensity, with organization and canalization and the production of intermediate clear spaces. Surrounding the posterior, and, to a lesser extent, the anterior tibial artery was a marked agglutinative process, the evidence of an extensive periarteritis. The artery, nerves, and veins were bound together into a dense conglomerate cord. In striking contrast to the above, was the peroneal artery, which throughout its course was macroscopically intact, without any sign of intimal or occlusive changes. The dorsalis pedis showed the general type of thrombus formation and did not differ from the above picture, except in the apparent lessened intensity of the process. The smaller arteries, such as the dorsalis hallucis, calcaneus, and plantar, showed very slight, if any, involvement, while the finer arterioles were apparently perfectly normal. Associated with the arterial condition was a striking coincident thrombophlebitis. Below the knee both the internal and external saphenous veins showed nodules of thrombotic origin. Surrounding the veins, as in the case of the arteries, were agglutinative changes suggesting a moderate periphlebitis.

The history of this case, from numbness and ischemia to gangrene, embraces roughly only eight months. It is interesting to note the evidence of an associated thrombophlebitis of the superficial veins.¹⁶ The clinical signs of superficial venous involvement were the few nodules along the course of the internal saphenous vein. The early symptoms of numbness and ischemia pointed to the beginning of an acutely progressive thrombo-angiitis obliterans, which later became more apparent by the appearance of trophic changes, culminating in gangrene.

After leaving the hospital the patient returned from time to time to the dispensary, complaining of pain and cramps in the left

¹⁶ Buerger, Jour. Amer. Med. Assoc., lii, 1319; International Clinics, vol. iii, ser. 19.

leg, more particularly in the left foot. About July 1, 1911, a dark blue discoloration appeared over the entire dorsum of the left foot, and the pain became so severe that the patient entered the hospital on July 12, 1911, and a week later was transferred to the surgical division. The patient insisted on operation as the only relief from the excruciating pain. On July 24 the left leg was amputated just above the knee by Dr. Peterson. The patient reacted well and his condition was satisfactory until the 29th, when, suddenly, he had a severe attack of vomiting and pain, which persisted unabated for the five succeeding days. Physical, gastric, and blood examinations were all negative, and on August 5, 1911, the patient died, apparently from exhaustion. Thrombotic occlusion of mesenteric vessels was thought possible, but, unfortunately, autopsy was refused.

Anatomical dissection of the amputated limb showed changes identical with those found in the right leg. The morbid process had not extended to such a severe grade of arterial occlusion, nor were the evidences of venous involvement so marked, although there was a moderate periphlebitis about the internal saphenous vein.

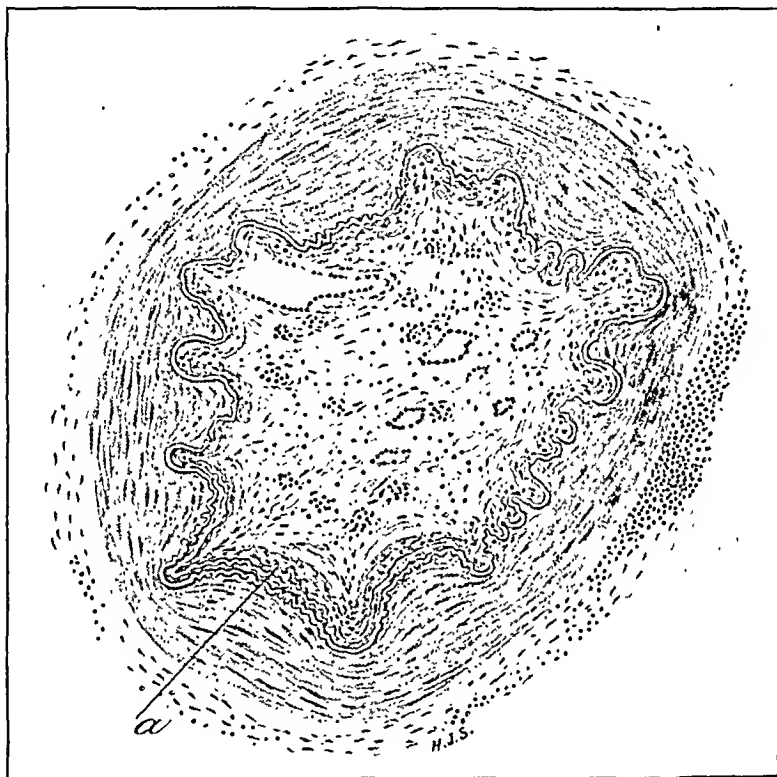
CONCLUSION. The type of gangrene represented by this case occurs in non-luetic young people,¹⁷ invariably men, with a low blood pressure, and before the age of marked angiosclerotic changes, hence, the name presenile or juvenile gangrene. The contention that this condition presents a fairly distinct clinical and pathological entity seems justifiable. Although it is true, as Huchard¹⁸ has shown, that we may have a marked arteriosclerosis with a low blood pressure, it seems extremely improbable that there is any marked sclerosis present in these cases. Histological study of the nerves and muscles from the affected areas showed neuritis and atrophy respectively. Careful study of specially prepared sections showed occasional proliferation of the elastic tissue lamina, characteristic of arteriosclerosis. There were no plaques nor crescentic lamellæ decreasing the caliber of the arteries such as we usually meet with in well-marked cases of angiosclerosis.

We were able to establish clearly, however, a proliferative process in the intima and to a slight extent in the subintimal tissue, leading to a considerable increase in the endothelial cells which encroached upon, and became part of, the organization and the periphery of the thrombus. In addition, we could clearly determine that there was a partial reduplication of the internal elastic tissue membrane which strongly suggested a pure arteriosclerotic process (see illustration). Buerger contends that such newly formed tissue is purely a coincident endarteritis and that the thrombus is primary

¹⁷ Leo Buerger and David J. Kaliski, *Med. Rec.*, New York, October 15, 1910.

¹⁸ *Monde Méd.*, October, 1909.

and the endarteritis secondary. However, if we believe that thrombosis does not occur in a normal vessel,¹⁹ and that an injured intima is necessary for thrombus formation, we have a more probable explanation for the obturating thrombus in a primary intimal change—arteriosclerotic—with consecutive thrombosis and organization of the thrombus. We found no evidence to support the idea of a gradually organizing mural thrombosis with eventual occlusion.



Thrombo-angiitis obliterans: Drawing from a section of the dorsalis pedis artery, showing occlusion of the lumen by an obturating thrombus in which the process of organization and canalization are well shown. Inferiorly (at *a*) there is well-defined evidence of proliferation of the endothelial cells and subintimal cells with partial reduplication of the internal elastic membrane.

That the actual occlusion is due to thrombosis there is hardly any doubt, but from our study we are of opinion that the question whether the thrombosis is the primary agent, whether the condition is a combined arteriosclerosis and thrombosis, or whether the condition is primarily due to neuritis is still an open one.

¹⁹ H. T. Brooks, General and Special Pathology. In press.

THE EFFECT OF CAFFEIN ON NITROGENOUS EXCRETION AND PARTITION.¹

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THE effect of caffein on nitrogenous excretion has been a subject of interest to investigators for some sixty years. Lehmann,² in 1853, found that under the influence of caffein there was a diminution in the excretion of urea amounting to 12 to 20 per cent. This was confirmed at first by other physiological chemists and supported, if it did not give rise to, the hypothesis that caffein lessens tissue waste. This specious phrase seems to have implied that caffein so increased the efficiency of the metabolic processes that a great economy in the consumption of nitrogenous matter was effected.

Unfortunately for this supposition subsequent work for the most part failed to confirm Lehmann's results; thus Hoppe,³ in carefully controlled experiments on dogs, found that caffein had no effect on the excretion of urea; Roux,⁴ in human beings, unaccustomed to the use of coffee, found a temporary increase in the amount of urea and other solid materials, while Le Blond⁵ obtained results corresponding with those of Hoppe. Reichert⁶ made use of the calorimetric method which he thought showed, beyond possible doubt, that caffein increased heat production and, as a corollary, increased destructive tissue metamorphosis. Dr. H. C. Wood,⁷ while agreeing that it does not "appear probable that caffein has any distinct specific influence upon protoplasmic nutrition" has pointed out that Reichert's results are not conclusive as regards nitrogenous metabolism.

Our work was not undertaken with any reference to this old controversy, but will be found (at least for small doses), to confirm by modern methods the position of those who denied any specific effect of caffein in economizing nitrogen.

Before describing our experiments we will refer to two "Dissertations," which have an indirect bearing on the subject of the

¹ Read before the Section on General Medicine of the College of Physicians of Philadelphia, October 23, 1911.

² Quoted by Reichert, q. v.

³ Arch. de Physiol. Norm. et Path., 1874, p. 578.

⁴ New York Med. Jour., April 26, 1890.

⁵ Deutsch. Klinik, 1857, vol. ix.

⁶ Paris Thesis, 1883.

⁷ Treatise on Therapeutics, 1894.

present paper, one by Schneider⁸ and the other by Rost,⁹ and both concerned with the fate of caffein in the animal body and its mode of elimination. The former found that it was largely decomposed in the organism, though it might appear in the urine if the dose were very large or the diuresis profuse. The latter found that after the administration of caffein as much as one-fourth of the amount ingested appeared again in the urine. It will be seen that our tables point to the latter conclusion as the correct one.

Our peculiar purpose was to observe the effect of various diuretics on the elimination of the total nitrogen, and particularly to investigate any deviation from the normal in the relative amounts eliminated as urea, uric acid, ammonia, creatine, purin bases, etc. In collaboration with Dr. Riesman we had previously studied the action of theophyllin from the same point of view, both in healthy persons and in nephritics.¹⁰ In the 2 normal cases reported here we used the greatest care in securing uniform experimental conditions and in employing the most accurate methods of analysis.

The Folin diet was employed largely because it gave us the advantage of comparing our figures with the results of his "Complete Analysis of Thirty 'Normal' Urines" (five persons¹¹).

The diet consisted of whole milk, 500 c.c.; "Horlick's malted milk," 200 grams; cream (18 to 22 per cent.), 300 c.c.; sugar, 20 grams; eggs (white and yolk), 450 grams; sodium chloride, 6 grams; water to make the whole up to 2 liters. Extra water to drink, 900 c.c. This diet represents 119 grams protein, 148 grams fat, and 225 grams carbohydrates, and yields 2800 (2786) calories, or enough for a man of 70 kg. (Voit).

The subjects of the experiment were fellow laboratory workers who had an intelligent interest in securing accuracy. In preparing the diet, certified milk was employed to insure as uniform a composition as possible. The methods of analysis were described in a previous article, in which one of us¹² collaborated, and may be enumerated as follows: Total nitrogen, Kjeldahl's method; ammonia nitrogen, Folin's method; urea, Folin's method; uric acid, Folin-Shaffer method; creatinin, Folin's colorimetric method; purin bases, combined Salkowski and Arnstein method (Welker); undetermined substances, by subtraction. Folin did not estimate the purin substances, and in his tables they are, therefore, included under the last-named heading.

The tables showing our results require little comment.

⁸ Dorpat, 1884.

⁹ Leipzig, 1895.

¹⁰ Philadelphia Gen. Hosp. Rep., 1911.

¹¹ Folin, Amer. Jour. Phys., vol. xiii, p. 45.

¹² Dittman and Welker, New York Med. Jour., May 15, 22, 29, and June 5, 1909.

TABLE I.—Case "W." Daily Records

Experi- mental day.	Volume c.c.	Specific gravity.	Reaction to litmus.	Ammonia nitrogen grams.	Creatinin grams.	Caffein grams.	Remarks.
PRELIMINARY PERIOD FOR DIET ADJUSTMENT.							
1							
2							
3							
NORMAL PERIOD.							
4	1200	1.025	Acid	0.6283	1.4840	0.00	
5	1895	1.020	Acid	0.6208	1.6684	0.00	
6	1270	1.024	Acid	0.6863	1.6073	0.00	
EXPERIMENTAL PERIOD.							
7	1108	1.029	Acid	0.7073	1.6318	0.390	Warm weather.
8	875	1.032	Acid	0.6370	1.6676	0.390	Very warm weather.
9	1070	1.030	Acid	0.6501	1.5205	0.390	

TABLE II.—Case "W."

Period.	Experimental days.	Total nitrogen.	Nitrogen of ammonia	Nitrogen of urea.	Nitrogen of uric acid.	Nitrogen of purin base.	Nitrogen of crea- tinin.	Nitrogen of un- deter- mined bodies.
PERIOD TOTALS.								
I	4th to 6th	45.7710	1.9354	39.6916	0.4785	0.0104	1.7694	1.8857
II	7th to 9th, caffein .	46.1960	1.9945	40.1325	0.3497	0.2330	1.7915	1.6948
DAILY AVERAGES.								
I	4th to 6th	15.2570	0.6451	13.2305	0.1595	0.0035	0.5898	0.6286
II	7th to 9th, caffein .	15.3987	0.6648	13.3775	0.1166	0.0777	0.5972	0.5649
PERCENTAGES ON THE BASIS OF TOTAL NITROOEN.								
I	4th to 6th	4.23	86.72	1.05	0.02	3.87	4.12
II	7th to 9th, caffein	4.32	86.86	0.76	0.50	3.87	3.67

TABLE III.—Folin's Results on the Diet Used in These Experiments (From the Analysis of 30 Normal Urines).

	Total nitrogen.	Nitrogen of ammonia.	Nitrogen of urea.	Nitrogen of uric acid.	Nitrogen of creatinin.	Nitrogen of unde- termined bodies.
AVERAGE DAILY EXCRETION.						
High limits	18.2	0.85	16.2	0.15	0.66	0.85
Low limits	14.8	0.55	12.8	0.08	0.50	0.41
Average	16.0	0.70	13.9	0.12	0.58	0.60
PERCENTAGE ON BASIS OF TOTAL NITROOEN (5 CASES).						
High limits	5.0	89.4	1.00	4.50	5.30
Low limits	3.3	86.2	0.60	3.20	2.70
Average	4.3	87.50	0.80	3.60	3.75

TABLE IV.—Case "M." Daily Records.

Experi- mental days.	Volume c.c.	Specific gravity.	Reaction to litmus.	Ammonia nitrogen, grams.	Creatinin, grams.	Caffein, grams.	Remarks.
PRELIMINARY PERIOD FOR DIET ADJUSTMENT.							
1							
2							
3							
NORMAL PERIOD.							
4	1770	1.019	Acid	0.6839	1.7921	0.00	
5	1492	1.022	Acid	0.8088	1.6790	0.00	
6	1480	1.019	Acid	0.6879	1.7630	0.00	
EXPERIMENTAL PERIOD.							
7	1190	1.024	Acid	0.5998	1.5806	0.390	
8	1770	1.019	Acid	0.6046	1.5252	0.390	
9	2368	1.017	Acid	0.6365	1.8268	0.390	

TABLE V.—Case "M."

Period.	Experimental days.	Nitrogen			Nitrogen of uric acid.	Nitrogen of purin base.	Nitrogen of crea- tinin.	Nitrogen of un- deter- mined bodies.
		Total nitrogen.	of ammonia	Nitrogen of urea.				
PERIOD TOTALS.								
I	4th to 6th, normal	50.549	2.1806	42.2994	0.4434	0.0709	1.9457	3.6090
II	7th to 9th, caffein	49.828	1.8409	44.0281	0.3872	0.2489	1.8336	1.4893
DAILY AVERAGES.								
I	4th to 6th, normal	16.8497	0.7269	14.0998	0.1478	0.0236	0.6386	1.2030
II	7th to 9th, caffein	16.6093	0.6136	14.6760	0.1291	0.0830	0.6112	0.3964
PERCENTAGES ON BASIS OF TOTAL NITROGEN.								
I	4th to 6th, normal	4.32	83.68	0.88	0.14	3.85	7.14
II	7th to 9th, caffein	3.70	88.36	0.78	0.50	3.68	2.99

Table I presents the "daily records" of Case "W." During the "Preliminary Period" of three days the diet was strictly adhered to, but no specimens were saved. During the normal and experimental periods daily estimations of ammonia nitrogen and creatine were made with the fresh specimen. The other estimations were made in combined "aliquot" samples at the end of each period. During the "Experimental" period the weather was very hot, and this, by producing diaphoresis, prevented any diuresis that might otherwise have occurred.

Table II. The first part of this table shows the total nitrogen for each period and the fractional portions for each constituent; in the case of ammonia and creatinin calculated from the previous table. In the second part these figures are reduced to daily averages. In the third part they are shown as percentages on the basis of the total nitrogen. Comparison with Folin's results in Table III fails to show the slightest deviation from the normal. The purin base nitrogen increased from 3.5 mg. to 77.7 mg., mani-

festly due to the ingested caffein which represents about 113 mg. of nitrogen.

Tables IV and V belong to Case "M" and are similarly constructed. The daily records show that there was a slight diuresis during the caffein period as a whole, probably not significant. The final tabulation in Table V again shows nearly normal figures. In the normal period there seems to have been some disturbance in metabolism manifested by a diminution in the percentage of urea and a corresponding increase in the undetermined substances. The normal relations were restored in the caffein period, but it is doubtful if we can attribute this to the drug. The purin nitrogen is here also increased (from 23 to 83 mg.), again corresponding to about half of the caffein ingested.

CONCLUSIONS: 1. In the amount given, corresponding to a small daily medicinal dose or to three ordinary cups of coffee, caffein produced slight if any diuresis.

2. The purin nitrogen was increased. This was due in all probability to the elimination of the caffein.

3. The total nitrogen remained unaltered and no abnormalities in the distribution of the nitrogen were observed, with the exception of the increase in the quantity of the purin nitrogen. Caffein in the doses given would therefore appear to exert no disturbing influence on nitrogen metabolism in man.

4. There was no evidence that caffein lessened tissue waste, in the sense of the older writers.

5. Clinical experience teaches us that large therapeutic doses of caffein produce diuresis. The effect of such large doses on nitrogen metabolism cannot be accurately predicted, but it would seem probable that no marked disturbance would result.

The work described in this paper was performed at the suggestion and under the direction of Prof. John Marshall. We desire to express here our appreciation of his kindly interest and suggestions.

REMARKS ON CARDIOSPASM, WITH SPECIAL REFERENCE TO TREATMENT AND THE USE OF THE ESOPHAGOSCOPE FOR EXAMINATION, BASED ON A STUDY OF SEVENTEEN CASES.

BY WILLIAM LERCHE, M.D.,
ST. PAUL, MINN.

By the "cardia" anatomists understand the junction of the esophagus with the stomach, indicated by a rough zigzag line where the pale pink mucous membrane of the esophagus unites with the deeper red mucosa of the stomach.

To the cardia has been ascribed the physiological closure of the esophagus toward the stomach, but recent experiments of Schreiber have shown that the "epicardia" is the part which effects this closure. By epicardia is understood the part of the esophagus from the cardia to about the hiatus esophageus, 4 to 5 cm. long, and comprising the abdominal and the diaphragmatic parts.



FIG. 1.—X-ray picture, showing pear-shaped dilatation of the esophagus from Case 1V.

The name cardiospasm, which was given by Mikulicz to the spastic closure of the lower end of the esophagus, naturally conveys the idea that the anatomical cardia is the only part affected, but I am convinced that this is not always so, because in a number of cases of so-called cardiospasm, which I have examined through the esophagoscope, I have found the epicardia to be involved in the spastic contraction. The name cardiospasm, therefore, seems

somewhat inadequate. I think that it is of importance to keep this in mind in the study of the pathological conditions in these cases, because otherwise one might be led to erroneous conclusions as to the nature of the obstruction encountered unless the esophagoscope is used in the examination. Thus, when the epicardia is spastically closed and the esophagus is dilated immediately above



FIG. 2.—X-ray picture of a dilated esophagus, the largest diameter of which is in the upper thoracic part.

the diaphragm forming a pouch against the bottom of which the examining sound strikes, tumor and twisting or angulation of the canal may be imagined to be the obstructive cause. If the epicardia was open the sound would more readily become engaged and easily overcome any resistance of the cardia.

I know of a number of cases in which the obstruction was thought

to be caused by a newgrowth, in which the esophagoscopic examination proved it to be due to cardiospasm and *vice versa*.

Strümpel, in 1881, reported a case in which he had made a diagnosis of dilatation of the esophagus due to angulation of the lower end of the organ. In this case Weigert made the postmortem and found no angulation nor other obstruction; it was an ordinary case of cardiospasm with dilatation.

A diagnosis of angulation *intra vitam* cannot well be accepted unless proved by esophagoscopic examination.

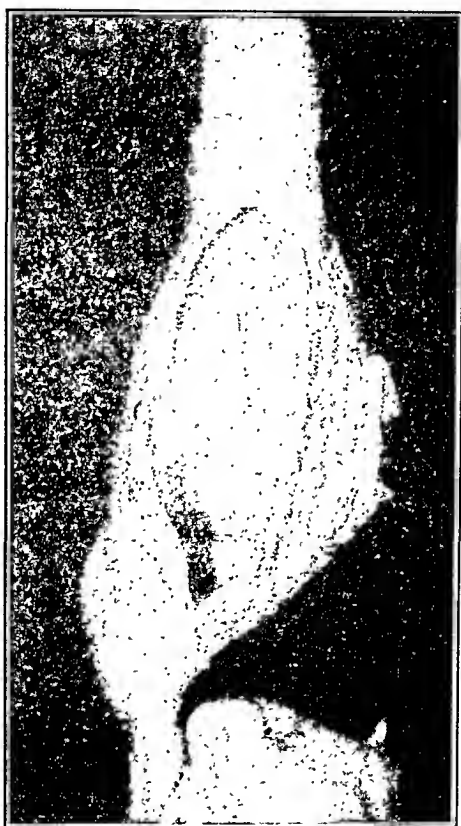


FIG. 3.—Specimen of an enormously dilated esophagus

The shape of the dilated esophagus varies in the different cases. The majority of cases that have come under my observation have had the largest diameter in the lower third, like Fig. 1, which I should call pear-shaped. Case II had the largest diameter in the upper thoracic part, which is unusual. (See Fig. 2.) Spindle-shaped, cylindrical, and bottle-shaped forms have been described.

Fig. 3 shows a specimen of an enormously dilated esophagus, which I had the opportunity to examine in the Pathological Institute in Vienna through the courtesy of Professors Weichselbaum and Gohn. The capacity of such a dilated esophagus may be

as high as one and one-half quarts. The mucous membrane is frequently the seat of chronic catarrh, and appears through the esophagoscope white and edematous, and at times shows inflamed red patches or streaks. Ulcers or scars therefrom may be present. The entire wall of the esophagus may be hypertrophied, the different layers participating in this, but particularly so the circular muscular layer. More rarely the esophageal wall is atrophic and appears to be thinner than usual. The epicardia-cardia is almost always found normal. The esophageal wall may be thinner in parts. The right wall is particularly prone to sag down on the diaphragm and form a pouch.

ETIOLOGY. Two groups of diffuse dilatation of the esophagus without anatomical obstruction can be recognized. In one, spasm of the cardia is primary and the dilatation of the esophagus secondary. The cause of the spasm may be disturbance in some neighboring organ or irritation along the pneumogastric nerve. A neurotic temperament plays an important part in some cases. In the other group atony of the esophageal wall is primary and the cardiospasm is secondary.

Kraus has described a case of a greatly dilated esophagus with cardiospasm, in which at postmortem changes in the pneumogastric nerve were demonstrated. In the left vagus less than one-half of the normal nerve bundles appeared to be intact. Any pathological process in the esophagus may give rise to cardiospasm. Cardiospasm secondary to a newgrowth, ulcers, etc., will not be discussed here.

Sex. In my series of cases 10 were men and 7 women.

Age. Cases of cardiospasm have been reported in early childhood. In one of my patients it started at the age of fourteen years. The oldest person that I have treated for cardiospasm was aged eighty-four years.

PROGNOSIS. Some cases of primary cardiospasm with diffuse dilatation of the esophagus seem to remain well after stretching. Others, apparently similar cases, will suffer a relapse. The etiology in each case must be taken into consideration in giving a prognosis. The treatment of cardiospasm by stretching has been in vogue only a few years and sufficient time has not elapsed to determine what percentage of cases will remain permanently cured. One writer recently made the statement that he had not seen any case of this kind that was not completely cured by dilating the cardia. Some time ago I had under observation a patient who had previously been treated for cardiospasm by this observer. The patient had recurrence of the trouble and was worse off than ever.

SYMPTOMS AND DIAGNOSIS. The initial symptoms vary somewhat. A sensation of choking while eating, immediately followed by regurgitation of food is the earlier manifestation in some patients. In others, a sensation of the food sticking behind the upper part of the

sternum and slowly passing down may be noticed now and then for months before a choking spell during meal with regurgitation of food comes on. One patient had severe burning in the throat, relieved by drinking cold water, for many months before regurgitation began. Later, these patients regurgitate some of the food and large quantities of slime at intervals after eating, and they will take large draughts of water with their meals, in order to force the food into the stomach. Sometimes there is a night cough due to aspiration of the esophageal contents during sleep. There may be considerable loss of weight.

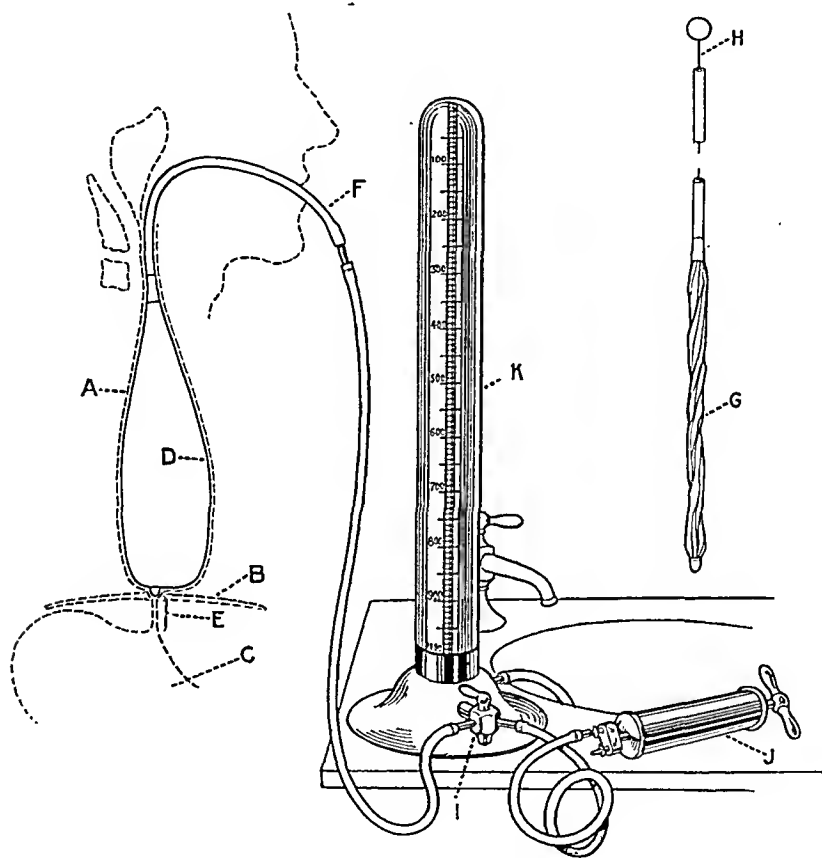


FIG. 4.—Author's esophagometer.

Pain in the chest or in the epigastrium is experienced by some. In one of my patients severe pain in the chest radiating to the back and both sides of the neck came on in paroxysms.

After a careful general examination a stomach tube stiffened by a wire stylet is introduced into the esophagus in order to measure the distance from the incisor teeth to the obstruction, and also to determine the resistance of the spastic epicardia-cardia. The stylet is then removed, and if there is any contents present in the esophagus it can be drawn off through the tube. The use of the tube

with the stylet saves the extra introduction of a sound. The next step is to measure the capacity of the dilated organ, which can be quickly accomplished by the use of my esophagometer (Fig. 4). This is done by introducing a large thin rubber bag (*G* and *D*), attached to a stomach tube, into the esophagus by the aid of a wire stylet (*H*), and then distending the bag with air (as suggested by Strauss), which is then drawn off and measured. By first turning the stopcock handle (*I*) toward the air-pump attachment and exhausting the air in the glass cylinder (*K*), the water from the bowl should fill the cylinder to the top of the inner glass tube. Then turning the handle toward the rubber bag attachment, the air pump is reversed and air is slowly pumped into the rubber bag in the patient's esophagus until the patient complains of pressure in the chest. If the handle is then turned toward the glass cylinder, the air in the rubber bag will be sucked into the cylinder. The number of cubic centimeters of air that the dilated organ will hold can then be read off on the scale. I first described this apparatus in the *St. Paul Medical Journal*, April, 1908, but have later modified it somewhat. In my work this method has been used for the purpose of estimating the size of the dilatation only, and not for making a differential diagnosis between a low-seated diverticulum and dilatation of the esophagus, as advocated by Strauss, because the two conditions may co-exist, hence the method might mislead. If desired, an x-ray picture may now be taken after filling the above-mentioned rubber bag with 10 to 20 per cent. subnitrate of bismuth suspended in some thick fluid. I use strained oatmeal gruel. The picture is then taken from right to left (Feehterststellung) or anteroposteriorly.

The most important step in the examination comes last, namely, the esophagoscopic examination of the organ. By the aid of the esophagoscope the distance from the incisor teeth to the obstruction can be measured, the capacity of the esophagus roughly estimated, the shape of the dilatation observed, and the presence of a diverticulum excluded.

As a matter of fact, the esophagoscope can supplant all the other above mentioned means of diagnosis. In addition, the condition of the wall of the esophagus can be studied through this instrument. The necessity of esophagoscopy in every case will at once be apparent when we know that the esophageal mucosa may be the seat of various lesions such as ulcer, newgrowth, acute or chronic catarrh, etc.; or the wall may be in a state of atony or spasm. The irritation from such lesions may cause recurrence of the spasm after the stretching, and the knowledge of their presence is, therefore, essential. Furthermore, stretching of the epicardia-cardia without first having excluded pathological lesions by inspection through the esophagoscope might prove disastrous.

As a rule, the sound will pass the spastic epicardia-cardia on

gentle, steady pressure. In 2 of my cases, however, the epicardia was so firmly closed by the sapsm that it did not admit the sound. The esophagoscope was introduced and the probe applied under the guidance of the eye, with the same result. I then rubbed the epicardia with a 10 per cent. cocaine solution on the cotton applicator, after which the epicardia-cardia opened and could be inspected. *In no case of cardiospasm is the epicardia-cardia impermeable.* Sounds of different pattern give very little dependable information in these cases; the esophagoscope is the only instrument by which a positive diagnosis can be made.

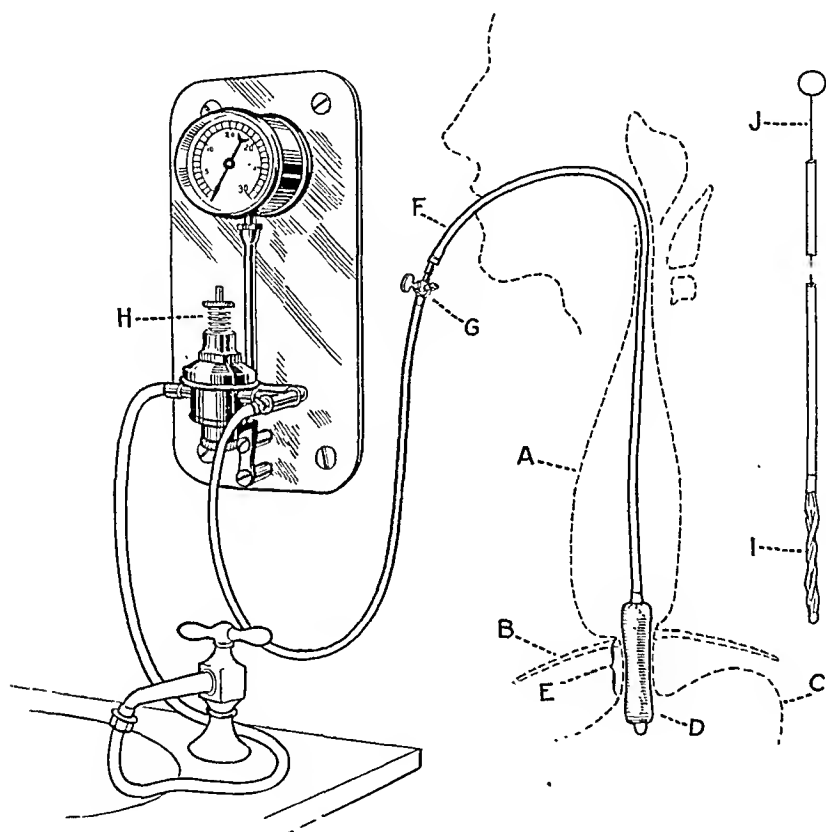


FIG. 5.—Author's apparatus for dilating the cardia-cardia.

TREATMENT. The routine treatment of cardiospasm is the stretching of the lower end of the esophagus. This is done by introducing into the cardia-cardia a silk-rubber bag (Russell) attached to a stomach tube and distending it forcibly with water or air, leaving the dilator *in situ* as long as the patient can stand it. As a rule, it cannot be endured more than a few minutes.

I make up the dilator in the following way: The distal end of a small-sized stomach tube with thick walls is closed and a number of holes are made in the lower four inches of the tube. Over this

is pulled an ordinary thin rubber condom, and outside of this a sausage-shaped bag 3 cm. in diameter and 15 cm. long, made of strong China silk. Both ends of the silk bag and the inner condom are securely fastened with a strong silk thread. Over the silk bag is pulled another condom to facilitate the introduction and prevent soiling of the silk bag.

The distance from the incisor teeth to the obstruction is noted and marked on the rubber tube. By the aid of a wire stylet (*J*, Fig. 5) the dilator is introduced into the epicardia-cardia and connected with the apparatus (Fig. 3), which is provided with a manometer and a pressure regulator (*H*). By slowly turning the screw of the regulator the pressure is gradually raised. The apparatus is modified from my first device, which I described in an article on Dilation of the Esophagus,¹ etc. About 10 pounds pressure is usually required for thorough stretching. When the dilatation is done the pressure is immediately relieved by turning the stop-cock (*G*). The regulator prevents a sudden high pressure and the manometer is essential to keep track of the pressure. More than 15 pounds pressure is liable to burst the silk bag. Von Hacker found the average diameter of the adult cardia 35 mm., and that of the esophagus at the level of the diaphragm 24 mm., when the organ was filled with plaster of Paris or wax. Therefore, when the diameter of the silk bag is 30 mm. it is safe to use as high pressure as the silk bag will stand. It may perhaps be safe to dilate the epicardia-cardia to 35 mm., but I have had good results with the 30 mm. limit, and I feel safer in not exceeding this in view of the fact that the average diameter of the esophagus at the upper level of the diaphragm is 24 mm. I do not consider the patient's expression of pain a guide to the amount of pressure to be used. The fact that the dilator cannot expand beyond a known limit is the safety guide.

In several cases of cardiospasm of many years standing I have given the epicardia-cardia one or two stretchings, followed by other treatment required, with the most excellent result. It has been my experience that when cardiospasm recurs after repeated stretching other treatment besides stretching is indicated. The latter treatment is a painful procedure, and should not be repeated unnecessarily.

For the treatment² of the catarrhal condition of the mucous membrane of the esophagus I have been using nitrate of silver in solution, injecting it through a fine silver cannula, which has little holes on the sides near the distal end, but has the end closed. The cannula is inserted into a thick-walled rubber tube in order that it may be easily introduced without injuring the passage

¹ AMER. JOUR. MED. SCI., October, 1907.

² Cuts of my instruments for application and other esophageal work appeared in *Surgery, Gynecology, and Obstetrics*, October, 1910.

(Fig. 6). The length of the instrument is 23 cm., so as to reach somewhat beyond the cervical portion of the esophagus. If ulcers are present they are best treated by direct applications through the esophagoscope of nitrate of silver melted on the applicator or of tincture of iodine.

For intra-esophageal application of the galvanic current in cases of atony of the esophagus I have devised an electrode, which can be introduced in a collapsed condition and expanded when it

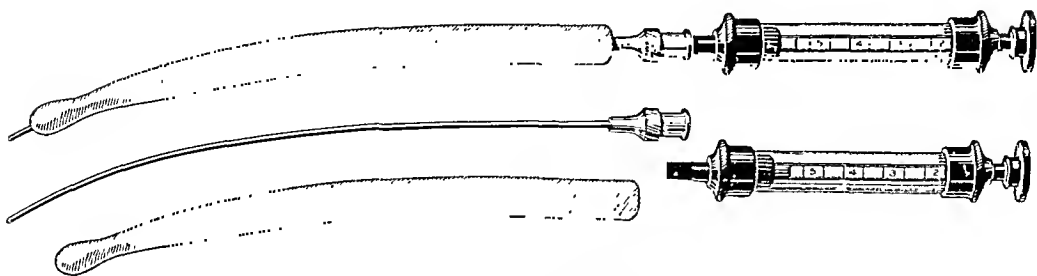


FIG. 6.—Author's esophageal syringe.

reaches the dilated part to be treated. The electrode collapsed and expanded is shown in Fig. 7, which illustrates well the working mechanism of the instrument, and the four thin steel springs (*A*) covered with felt to transmit the current. The handle is made of hard rubber and the long shaft of spiral steel wire is covered with a rubber tube.

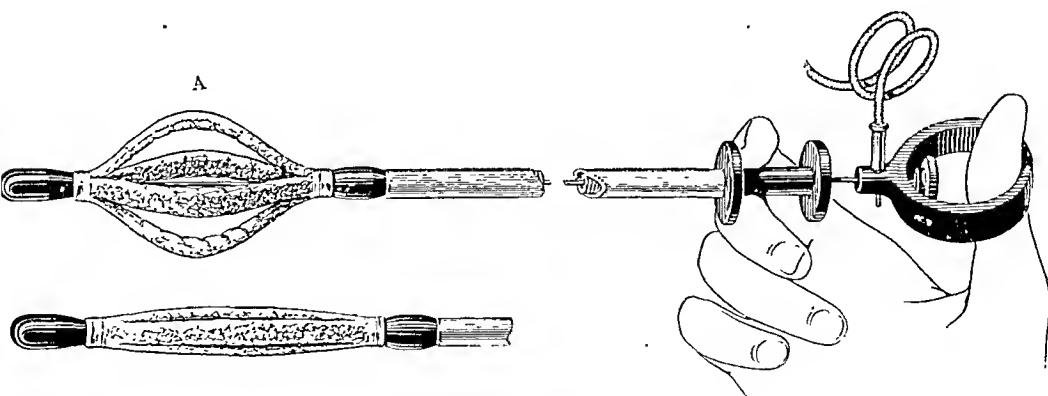


FIG. 7.—Author's esophageal electrode. Four thin steel felt-covered springs are shown at *A*.

The examination as well as the treatment by stretching in cases of cardiospasm can be done in the office.

Thoracotomy would, in my opinion, not be indicated unless the causative factor was definitely known to be in the thorax, and the simple treatment outlined above had failed.

Gastrotomy for mere stretching the epicardia-cardia is not justifiable, because more than one dilatation is often needed.

Furthermore, stretching performed through the mouth can be done quickly and without incapacitating the patient for work.

Seventeen cases of cardiospasm have come under my observation, and of these, 16 have been studied through the esophagoscope. For this article I have selected 4 cases, the first of which is the typical form of chronic cardiospasm. The other cases present features that differ somewhat from the ordinary.

CASE I.—Male, aged twenty-seven years. Ten years previous to consultation the patient had a choking spell while eating, with regurgitation of food. Ever since he has had difficulty in swallowing his food, and has had to take large quantities of water with which to force it into the stomach. He frequently gulped up food and slimy fluid. At times he had pain behind the lower part of the sternum.

Examination. Sounds met an obstacle at 42 cm. from the incisor teeth, which was passed without difficulty. The esophagus held more than a pint of fluid, and when the patient drank a couple of tumblerfuls of water he could regurgitate the whole amount a few minutes later, with the greatest of ease. The stomach contents was normal.

Treatment. The epicardia-cardia was stretched twice with the 3-cm. dilator. The patient has remained well since the last treatment, which was given four and one-half years ago. About three years after treatment I had the opportunity to examine the patient with the esophagoscope and found a perfectly normal appearing esophagus and the epicardia-cardia opened and closed rhythmically as in health.

The muscular tone of the esophagus must have been well retained in this case, because the patient could practically empty the organ by regurgitation after taking nearly a pint of fluid.

CASE II—Female, aged twenty-two years, unmarried. At the age of eighteen years, while eating a banana, a piece of it stuck in her throat. On drinking water it passed down. After this, whenever she ate, the patient noticed that the food would stick high in the chest and pass down slowly. Several months later it became difficult to get anything into the stomach and she had to take large draughts of water with which to force down the food. She had no pain, but an occasional burning sensation in the chest after gulping up mouthfuls of food and slime. She did not regurgitate often and it did not come easy, as it does in most cases of cardiospasm with dilatation.

Examination. Obstruction met 40 cm. from incisor teeth, which yielded to gentle pressure of the sound. Capacity of the dilated esophagus measured by the esophagometer was 400 c.c. X-rays (see Fig. 2) showed a sausage-shaped dilatation with the largest diameter in the upper thoracic part.

Esophagoscopic Examination. The mucous membrane was paler than normal, and near the epicardia it was deeper red than normal. The epicardia was closed. The upper thoracic part of the esophagus was ballooned out in an unusual manner, the like of which I have not seen in any other case.

Treatment. The epicardia-cardia was stretched several times with the 3-cm. dilator. The patient felt some relief, but was not entirely well; there was a sensation as if the food stuck in the upper part of the chest and passed down slowly. Repeated esophagoscopic examinations later on revealed the same ballooning of the upper thoracic portion of the esophagus as before.

The patient returned two years later in about the same condition. There was not so much obstruction to the passage of food at the lower end of the esophagus, but it passed slowly through the upper part. Esophagoscopic examination showed that the lower thoracic part had perhaps contracted somewhat, while the upper thoracic portion was in the same condition as it was two years previously. Although skeptical as to its value, I decided to try the application of the galvanic current intra-esophageally to the upper thoracic part, because this portion of the organ was undoubtedly in a state of atony. It would be impossible to bring an ordinary straight electrode in contact with the bulging walls of the esophagus, and I therefore, devised the above-described instrument (Fig. 7). After twenty applications esophagoscopic examination showed a surprising improvement, and after ten more applications the epicardia-cardia was stretched. Two months later esophagoscopic examination was made and the esophagus found practically normal, the cardia opening and closing rhythmically as in health. The patient felt entirely relieved. Seven months later esophagoscopic examination was again made and the organ found to be functioning normally. More than one year after treatment the patient was feeling perfectly well.

In this case there was primarily atony of the upper thoracic part of the esophagus, which delayed the passage of food and thereby irritated the epicardia-cardia to spasm.

CASE III.—Female, aged twenty-three years, married, one child, three miscarriages, and one extra-uterine pregnancy, for which I operated upon the patient. One year after the extra-uterine pregnancy I performed supravaginal hysterectomy.

She had much trouble with her stomach in babyhood and was never strong. When aged ten years she was taken out of school on account of epigastric pain and belching of gas. At the age of sixteen years she experienced a severe cramp-like pain in the chest and between the shoulders. At the age of eighteen years, during the seventh month of pregnancy, she had a sensation of choking and oppression in the chest on eating, and shortly afterward she commenced to regurgitate her food. Occasionally she had pain

in the chest. At times fluid mixed with food came through the mouth and nose during sleep. She had been treated elsewhere by stretching of the cardia. The patient was fairly well for a while after the treatment, but the symptoms returned with regurgitation of food and severe attacks of pain. The pain would come on suddenly deep in the chest, radiating to the back between the shoulders and up the neck. Sometimes it was felt behind the

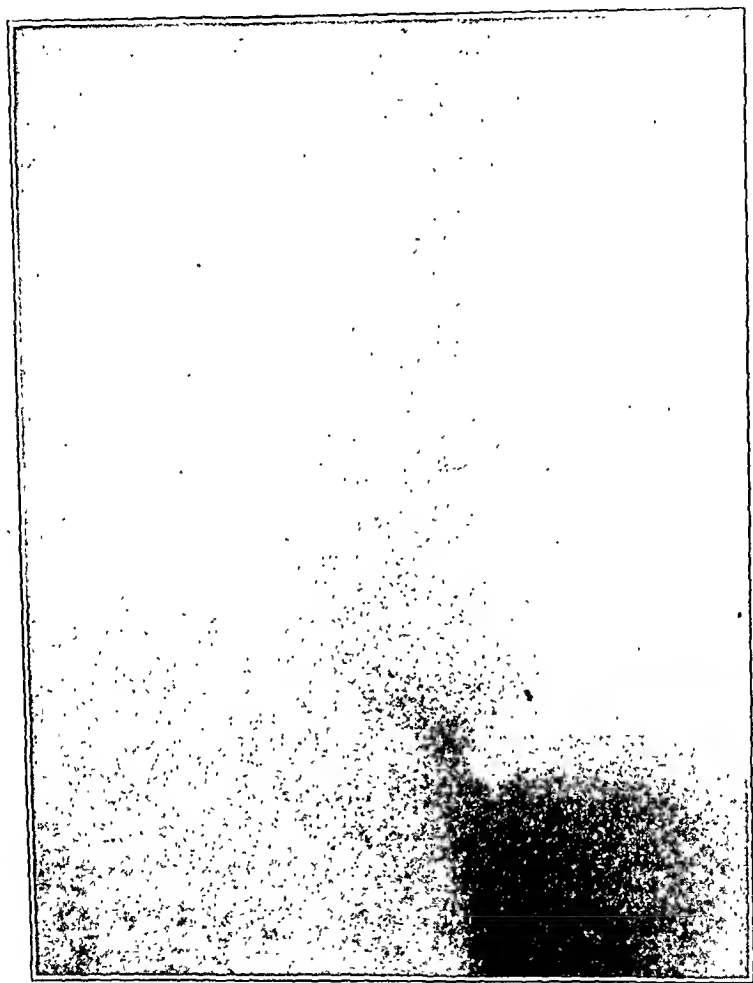


FIG. 8.—X-ray picture from Case 111, showing relation of dilated esophagus to epicardium and stomach.

ears, particularly on the right side. The pain was cramp-like in character and so severe at times that repeated hypodermics of morphine would be required to relieve the patient. At times she felt as if everything in her chest was thumping. She had to take large quantities of water to get down her food.

Examination. Obstruction met at 40 cm. from incisor teeth, which offered some resistance to the sound. A considerable quantity

of slimy fluid with particles of food was drawn off. The capacity of the esophagus measured by the esophagometer was 500 c.c. The x-ray picture of the case (Fig. 8) is interesting because it illustrates beautifully the relation of the dilated esophagus to the epicardia and the stomach. It was due to an accident that this picture was obtained, the rubber bag containing the bismuth mixture dropped partly into the stomach.

Several esophagoscopic examinations were made and the mucous membrane showed signs of chronic and acute catarrh. On one occasion I found the upper two-thirds of the esophagus contracted, and the walls had to be pushed apart with the instrument. In the lower part above the epicardia was found about 100 c.c. of slimy fluid and the epicardia was firmly closed. The patient had just then had severe attacks of cramps in the chest, and the entire esophagus was apparently in spasm. At another examination I also noticed a tendency to contraction of the esophageal walls, but again on other examinations the esophagus was found open.

The epicardia-cardia was repeatedly stretched, which gave relief for a while. However, the spasms soon returned. Marital troubles and excitement would precipitate attacks, but, on the other hand, attacks came on without any apparent provocation. During the attacks I observed that the pulse was slow—about 60. I then tried the administration of $\frac{1}{150}$ grain of atropine sulphate three times daily for two weeks, with good result. There were no attacks of pain or regurgitation for several months. The use of atropine here was based upon the results of the experiments of Langley.³ When the trouble recurred several months later it was in a mild form, with but little pain and only occasional regurgitation. Dilatation of the epicardia-cardia was again tried.

The patient subsequently died of pneumonia with complications. Partial postmortem was made and the esophagus found to be normal in size and appearance. On inflating the organ with air, however, it was found that it could readily be distended to several times its size, indicating that a dilatation had been present at a comparatively recent date.

My impression was that in this case there was an irritation of the pneumogastric nerve somewhere, but the neurotic temperament of the patient undoubtedly was an important factor.

CASE IV.—Female, aged twenty-six years, unmarried. At the age of fourteen years the patient became subject to frequent attacks of a burning and gnawing sensation in the throat above the sternum and also behind the upper part of the sternum. The following year she noticed that coarser foods, such as corn, cabbage and beans, would stop in the chest, causing a sensation of pressure, and would then be regurgitated. In a few months liquids acted

in the same manner. She gradually learned to force the food down with water, and in the years that followed had no trouble with regurgitation so long as she took only a small amount of food at a time. She could not take iced water or charged drinks. The burning in the throat could be relieved on drinking cold water.

Examination. Obstruction met with at 42 cm. from incisor teeth, which did not permit the passage of the sound; 250 c.c. of slimy fluid with particles of food were drawn off. The capacity of the esophagus was 550 c.c. The x-ray picture (see Fig. 1) shows a pear-shaped dilatation with a pouch at the bottom.

Esophagoscopy. The esophagus appeared like a rigid tube with immovable walls. The greatest diameter was just above the epicardia, and the right wall of the organ was flattened out over the diaphragm, forming a pouch, the bottom of which the examining sound encountered. The mucosa was glassy white and edematous with red streaks here and there. The epicardia was so firmly closed that the esophagoscopic tube or the probe could not be pushed through. After the application of cocaine solution the epicardia opened. The mucous membrane of the latter was darker red than normal. The left wall of the esophagus was quite straight, so that the dilatation appeared to be more at the expense of the right wall.

Treatment. After one stretching with the 3-cm. dilator the patient reported four weeks later that there was no hindrance to the food whatever, but the burning in the throat continued unabated. I therefore commenced with daily injections of nitrate of silver solution into the upper thoracic part of the esophagus, but without any apparent effect. The injections were then made into the cervical part, and the patient soon reported decided improvement. She remained well for one year, with the exception of occasional burning sensations. She then noticed slight retention of food if she ate hurriedly. She therefore had another treatment by stretching, one and one-half years after the first treatment.

The cause of the severe burning in the throat, which acted like heartburn, is not clear, as the mucosa in the cervical part appeared quite normal. The chronic catarrh of the thoracic portion may have been the cause of it, but the decided improvement after the injections were made into the cervical portion made me think that the latter part was at fault. Shaffer has described "the upper cardiac glands of the esophagus," situated laterally in the upper end of the esophagus. These glands are of the same type as the acid-secreting cardiac glands of the stomach. The possibility occurred to me that these glands might have had something to do with the burning, but I could not demonstrate any reaction through the esophagoscope.

CONCLUSIONS. 1. If by cardiospasm is understood spasm of the anatomical cardia only, the name is not adequate.

2. The etiology of cardiospasm is obscure in some cases, and one should, therefore, be cautious in giving a prognosis.

3. Each case of cardiospasm must be studied *per se* and treated accordingly. Simply to demonstrate a spastic obstruction with the sound and stretch the epicardia-cardia is not sufficient in all cases.

4. The esophagoscope is paramount in making a correct diagnosis in any esophageal disorder.

The x-ray pictures have been taken for me by Dr. W. S. Fullerton, of St. Paul.

REVIEWS

SURGICAL APPLIED ANATOMY. By SIR FREDERICK TREVES, F.R.C.S., Sergeant-Surgeon to H. M. the King, late Lecturer on Anatomy at the London Hospital. New (sixth) edition, thoroughly revised. Pp. 676; 137 illustrations, of which many are in colors. Philadelphia and New York: Lea & Febiger, 1911.

TEN years ago we said of a previous edition of this work—revised then by the author with the assistance of Mr. Keith—that it was “prized by medical students for its lucidity, brevity, and, withal, its comprehensiveness.” We added: “We know of no book between whose covers is compressed so much valuable information in such an attractive style.”

The lapse of years has not made either of the above statements incorrect as applied to the present edition. Care has evidently been bestowed upon the revision and a number of additions have been made, but the clearness and precision of the original anatomical and surgical descriptions—to which it owed much of its success—are still noticeable. The defective proofreading of some of the earlier editions has been remedied and there is evidence of careful work in this direction. For example, the statement that the thyroidea ima artery “exists in 10 per cent. of all cases” is changed to “is found in one subject out of every ten.”

As to additions, they are found chiefly, as the preface states, in relation to the glands of internal secretion, to the lymphatic system, to the anatomy of the abdomen, and to new facts regarding the human body that have been revealed by the *x*-rays. Taking illustrations almost at random, we find described the development and anatomy of the pituitary body and its relation to acromegaly and gigantism; the pancreatic islets of Langerhans, and their bearing upon diabetic conditions; the suprarenal bodies, their growths and their involvement in renal tumors; the relations of stimulation of the laryngeal nerves to increased thyroid secretion; the atrophy and occasional disappearance of the parathyroids with advancing years; visceroptosis (with a diagram); the anatomy of the “Talma-Morrison operation;” gangrene of the intestine from embolism of the portal vein; and many other important and more or less recent additions to anatomico-surgical knowledge.

It is a pity that the diminishing but still noticeable tendency of many English surgeons to limit their field of inquiry to Great Britain and the Continent is not absent from this book. Many examples of this could be adduced, but we may mention the statement, under "Fractures of the Head or Neck of the Radius," that "the lesions if limited to the head could hardly be diagnosed," no allusion being made to the enlightening research of T. T. Thomas; and the more important omission of any reference to the Allis method of reducing hip dislocations, the antiquated and dangerous plan of "circumduction" being the only one described. If in the next edition Mr. Keith will supply such deficiencies as these, the book is likely to remain for many years what it has been since its first appearance, the most admirable and useful condensation of the subject of applied anatomy in the English language.

J. W. W.

DUODENAL ULCER. By B. G. A. MOYNIHAN, M.S. (Lond.), F.R.C.S. Pp. 179; 63 illustrations. Philadelphia and London: W. B. Saunders Company, 1911.

IN this monograph Moynihan has considered the subject of duodenal ulcer in an exhaustive and most interesting manner. The book consists of chapters upon ulceration in cases of burns or scalds, uremic ulcer, tuberculous ulceration, and the pathology, symptoms, diagnosis, and treatment of chronic duodenal ulcer, together with its various complications. This occupies 250 pages, and the remainder of the book, amounting to something over 100 pages, contains a detailed statement of all cases operated upon to the end of 1908.

There is but little to remark about in the book; it simply details in a complete and interesting way the phenomena of duodenal ulcer. The skill of the author as a surgeon is well known; he is one of the best of the abdominal surgeons of today, and his experience has been sufficiently great to make what he says authoritative. His skill is illustrated by his results; the mortality of the series of cases up to the end of 1909 was 1.6 per cent., and among the last 121 cases there were no deaths. Most of the cases were followed after operation, and it was found that practically 80 per cent. were cured, and only one patient was classed as being no better. One statement in the chapter on diagnosis (p. 112) should be memorized by every practitioner. He states that he has "never operated upon a case of retractive or recurrent 'hyperchlorhydria' without finding a duodenal ulcer." Another interesting statement is made when he says that he does "not believe in the duodenal ulcer which cannot be demonstrated to the most skeptical assistant or onlooker; the ulcer is always a visible, tangible, demonstrable lesion."

The only adverse criticism that might be made is that the size of the book could be materially reduced by eliminating the padding by unimportant case histories. Many of the illustrations are not up to the usual standard of the publishers. G. P. M.

A TEXT-BOOK OF MEDICAL DIAGNOSIS. By JAMES M. ANDERS, M.D., Professor of the Theory and Practice of Medicine and of Clinical Medicine, and L. NAPOLEON BOSTON, M.D., Adjunct Professor of Medicine, Medico-Chirurgical College, Philadelphia. Pp. 1195; 443 illustrations, 17 in colors. Philadelphia and London: W. B. Saunders Company, 1911.

To write a satisfactory work on medical diagnosis is a task of large proportions. Complete success has not, we believe, been accomplished in any first edition. The book before us is an attempt to present to the reader in reasonably condensed form the most approved modern methods of bedside and laboratory diagnosis, and this has, for the most part, been satisfactorily accomplished. The work is, nevertheless, susceptible of numerous improvements. Without wishing to be carping in our criticism we, however, feel that numerous additions, corrections, and alterations could advantageously be made in future editions.

We failed to find any allusion to sacro-iliac sprains, even in the discussion of lumbago, and no mention of cervical ribs. The modern classification of the cardiac arrhythmias receives but meagre consideration. No reference could be found to sinus arrhythmia, auricular fibrillation, pulsus alternans, nor to extrasystoles, although the latter is indefinitely alluded to in a brief paragraph on the "intermittent pulse." The statement that "the combination of symptoms known as 'heart-block' is only seen in cases in which the bundle of His is involved in a diseased process," requires modification, inasmuch as six or seven "exceptions" are on record.

We could find no mention of hepatic murmurs. Under sphygmographs only the obsolete Dudgeon and the Jacquet are alluded to. The time marker in the latter is said to record two-fifths instead of one-fifth of a second. The credit of devising the auscultatory method of determining blood pressure is given to "Karotskin," probably a misprint for Korotkow, while Fellner is not mentioned.

Under blood pressure only one type of instrument is alluded to. It would seem that the Erlanger and the Pachon instruments, at least, require mention. The determination of venous blood pressure should not have been ignored.

In discussing the newer methods of applying the tuberculin test the possible danger of the ophthalmic method should have

been mentioned, and the relative worthlessness of the v. Pirquet reaction in adults pointed out. For completeness the Moro reaction might have been included.

The index requires further elaboration. One seeks in vain for "pulsus paradoxicus," "vocal resonance," "pectoriloquy," and many other terms which must be sought under different headings. Kercher's name is spelled "Kearcher."

Pathological definitions heading the diseases are a useful addition to the text, but we question the advisability of introducing so many space-consuming "illustrative cases." The anatomical reasons for the normally greater right-sided pulmonary tactile fremitus should have been mentioned.

The chapters on diseases of the nervous system and Röntgenology are written by T. H. Weisenberg and G. E. Pfahler respectively, and are, so far as the reviewer's limited knowledge goes, satisfactory.

The work is attractively gotten up, with good print, many excellent illustrations, and with tables of differential diagnoses, which are probably useful for students. Among the illustrations the introduction of moving pictures in different nervous diseases may be mentioned. On the whole the aim of the authors to combine a description of different methods of physical, clinical, and laboratory diagnosis as available for different pathological conditions has been successfully consummated. G. W. N.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital, etc., Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia. Vol. IV; pp. 326; 35 illustrations. Philadelphia and New York: Lea & Febiger, 1911.

THE final volume of *Progressive Medicine* for 1911 opens with a painstaking review of diseases of the digestive tract by R. S. Lavenson. After he considers the esophagus, he takes up the pathological physiology as well as the diseases of the stomach. He then discusses diseases of the intestines. That appendicitis continues to excite interest and controversy is evident from the amount of space devoted to this subject. The peritoneum, the liver, and the biliary tract are next considered, particular emphasis being laid upon cholelithiasis. Lavenson's article of 92 pages concludes with a discussion of diseases of the pancreas.

A short contribution of 15 pages on diseases of the kidneys is furnished by John R. Bradford. The function of the glomerulus, the genesis of dropsy in heart disease and in Bright's disease, and a summary of the efficacy of urinary antiseptics, are among the important subjects covered in this contribution.

Genito-urinary diseases proper are thoroughly discussed by Charles W. Bonney in an article 45 pages in length. Functional renal diagnosis, unilateral hematogeneous infection of the kidneys, gonococcic infection of the kidney, and tuberculosis of the genito-urinary tract; intraperitoneal rupture, tumors and tuberculosis of the bladder; together with an extensive discussion of hypertrophy and carcinoma of the prostate and various conditions of the external genitalia are among the most important subjects considered.

A truly critical review of certain phases of general surgery is contributed by Joseph C. Bloodgood. Under the title of injuries this writer enters into an excellent discussion of shock and anesthesia, paying particular attention to the anatomical basis of shock as advocated by Crile and his associates, and to nitrous-oxide-and-oxygen anesthesia, which, it would appear, continues to gain in favor. A consideration of wounds, infections, lymphangitis, lymphadenitis, tetanus, and tumors is followed by a discussion of fractures, bone tumors, and advances in the surgery of the lymph glands.

The volume ends with an interesting contribution of 43 pages by H. R. M. Landis upon recent progress in therapeutics. In this distinctly practical chapter, Landis takes up not only the newer ideas in regard to drugs, but also lays particular emphasis upon such valuable therapeutic measures as rest, climate, diet, exercise, massage, hydrotherapy, and serum and vaccine therapy.

Considered as a whole, the four volumes of *Progressive Medicine* that have appeared during the past year furnish, without a doubt, the most complete and useful critical review of present-day medical thought that can be found in English.

G. M. P.

THE PRINCIPLES AND PRACTICE OF BANDAGING. By G. G. DAVIS, M.D., Member of the Royal College of Surgeons, England; Professor of Orthopedic Surgery, University of Pennsylvania. Third edition; pp. 128; 164 illustrations. Philadelphia: P. Blakiston's Son & Co., 1911.

THE author has given in this book an excellent explanation and illustration of bandaging. This the third edition is practically a new book, being rewritten from the older work. It is especially

designed for beginners and is, for that reason, well recommended for the use of students.

The text is clear and the style agreeable for a book of this sort. The illustrations clearly show what is fully explained in the context, and, being original with the author, point out admirably the points difficult for beginners. Every important bandage has a cut showing the turns and the method of application step by step. Brief mention is made of rubber and plaster of Paris. The handkerchief or triangle bandage is discussed and illustrated at great length.

For students, this work is most complete and easily on a par with any other work on the same subject. It is of a handy size and the type is clear and easily read. The placing of numbers on the various turns of the bandage in the difficult figures renders it much easier to master the method of applying the bandage illustrated.

E. L. E.

THE MODERN DIAGNOSIS AND TREATMENT OF DISEASES OF CHILDREN. By HERMAN B. SHEFFIELD, Instructor in Diseases of Children at the New York Post-Graduate Medical School and Hospital, etc. Pp. 619; 150 illustrations. Philadelphia: F. A. Davis Co., 1911.

THIS book, like the previous contribution of the author (the translation of Graetzer's *Pediatrics*), contains a generous amount of useful information. Unlike the earlier work, however, the present volume has its subject matter well arranged; it is well written; it is illustrated; most of the illustrations are original and most of them are excellent. In the main, the tone of the work is thoroughly scientific, and the newer methods of diagnosis and treatment are clearly and concisely described. The use of prophylactic and curative sera and of vaccines is dealt with in a judicial manner. The book making is well executed and the type is large and clear.

We detect few important omissions and fewer mistakes. Although he speaks of the importance of light percussion in children, Sheffield does not mention the value of finger-nail percussion in the young, nor does he lay stress upon the still more important matter of the "resistance" offered to the pleximeter. He does not differentiate between Cheyne-Stokes respiration and grouped cerebral breathing.

Although he does use the adjective mammary, as applied to the nipple line, instead of the questionable adjective mammillary, we find him describing the iliac region as the inguinal region. Others have objected, as do we, to so extending the limits of the groin.

The author deals with the subject of rectal examination, but he does not lay enough stress upon the digital examination of this

important region, nor does he mention all of the clinical findings that may be so elicited.

In the directions for making buttermilk, nothing is said about churning the soured milk. Thus the butter fats are left in, at least one is allowed to suppose so, and the resulting product is not buttermilk.

The Wassermann reaction, of which a full and lucid account is given, is not found in the chapter on "Diagnosis," but in that dealing with the "Treatment and Cure of Disease." The same criticism may be made of the description of the Widal reaction. Some minor objections might be advanced to the arrangement of the "Communicable Diseases." Thus we find diphtheria "sandwiched" between two of the exanthemata—scarlet fever and measles.

We should hesitate to believe that masturbation is often taught children by "erotic governesses," though we would admit that it is sometimes taught them by ignorant or vicious nursery maids.

However, most of the criticisms are minor ones, and we find little to invalidate the usefulness of the book. It is a good book, and we recommend it cheerfully to students and practitioners.

J. H. McK.

A MANUAL OF MATERIA MEDICA FOR MEDICAL STUDENTS. By E. QUIN THORNTON, M.D., Assistant Professor of Materia Medica in the Jefferson Medical College, Philadelphia. Pp. 525. Philadelphia and New York: Lea & Febiger, 1911.

THORNTON'S *Materia Medica* is a highly useful book, both for the practitioner and the student of medicine. It is divided into three parts: The first deals chiefly with the principles of prescription writing; the second contains the official remedies arranged alphabetically according to source and derivation; the third is a strictly alphabetical table of all the official preparations. In the second part the methods of preparation, the physiological and toxicological actions, and the uses of the various remedies are described in a strictly objective way, without any comment as to their relative value. This part will be found exceedingly useful by the practitioner who wishes to inform himself quickly as to the action and dose of a drug, and of the best way to administer it. The last feature, about which the medical profession is generally quite ignorant, receives careful attention in the case of nearly every preparation. An occasional non-official remedy is introduced, as for example salvarsan. Considering, however, the extensive employment of synthetic compounds, many of which possess unquestioned value, it would enhance the usefulness of the book if in future editions a section on these newer unofficial remedies was added.

D. R.

CASE HISTORIES IN NEUROLOGY. By E. W. TAYLOR, A.M., M.D., Instructor in Neurology, Harvard Medical School; Assistant Physician, Department of Neurology, Massachusetts General Hospital; Visiting Neurologist, Long Island Hospital, Boston. Pp. 305; 37 illustrations. Boston: W. M. Leonard, 1911.

IN brief, this book contains histories of more or less typical cases of nervous disease which are presented first as to history, then diagnosis, and finally, prognosis and treatment, and which are used by the medical students of Harvard University. The reviewer has known of this work for a number of years and from personal knowledge knows that the case history system has been instrumental in good work. This method has also been used in other specialties such as pediatrics and in medicine and surgery and is to be heartily commended.

T. H. W.

CLINICAL PATHOLOGY IN PRACTICE. By THOMAS J. HORDER, B.Sc., M.D., F.R.C.P. Pp. 216. London: Oxford Medical Publications, 1910.

THE task of the reviewer lies, not infrequently, in unpleasant pastures, beside waters that he feels should be dammed, which, were his preferences consulted, he would have done by someone else. The present reviewer keeps continually before his mind the fact that any book, no matter how small, is conceived of no hasty thought, and is born after much wearisome and fatiguing travail. He remembers this, and tries to view even a misshapen child, as the parent views it, with a kindly eye, seeing naught of its ugliness, but affectionately emphasizing each good trait.

The work at present under consideration has for its object "to present the practitioner with a brief survey of the scope and usefulness of modern pathological methods as applied to the diagnosis and treatment of disease." An introduction of nine pages is then devoted to a defence of laboratory methods and to an attempt to point out the proper correlation of the findings of the clinician and of the laboratory worker. Both the aim of the book and the introduction seem to us as smacking of a very early era in medicine, and as not being apropos in this day of our generation.

Granting that the aim of the author is a praiseworthy one, we fail to see that he hits the mark. Occasionally he strikes the target, but they are glancing shots, and do no one much good. We might cite instances of these stray half-hitting attempts, but they must be apparent to every one.

The volume presupposes ignorance on the part of the clinician

as to the features which should be studied in a case, and it shyly hints at what might prove of help. These hints leave us with the sensation of being suspended in midair, as it were, since we can not find a footing for our scientific groping feet. A much better idea of the usefulness of the application and advantages of clinical pathology is to be had from any of the numerous works devoted to this department of medicine.

E. H. G.

MENTAL MECHANISMS. By WILLIAM A. WHITE, M.D., Supt. Government Hospital for the Insane, Washington, D. C.; Professor of Nervous and Mental Diseases, Georgetown University, Washington, D. C.; Professor of Nervous and Mental Diseases, George Washington University, Washington, D. C.; and Lecturer on Insanity, U. S. Army and U. S. Navy Medical Schools. Pp. 515. New York: Journal of Nervous and Mental Disease Publishing Co., 1911.

As the author states in his preface, "This work is the result of a need growing out of my efforts to bring certain principles in the field of psychology to the younger members of my staff," and is an excellent presentation of the modern trend of psycho-analysis. The author has the gift of clear concise expression, and one who is not familiar with psycho-analysis, especially Freud's methods, will gain much from perusal of this work.

T. H. W.

LEITFADEN DER ELECTRODIAGNOSTIK UND ELECTROTHERAPIE, VON DR. TOBY COHN, Nervenarzt in Berlin. Pp. 212; 65 illustrations, 6 colored plates. Berlin: S. Karger, 1912.

THE popularity of this little guide is obvious from its previous translation into English, Italian, and Russian. In this fourth edition, the text is entirely rewritten and considerable new matter is added. Mention is made in the preface, of the author's writings in collaborate works, upon electricity in conjunction with mechanotherapy (massage and gymnastics), but the latter is not considered in this text.

The section on electrodiagnosis contains six admirably arranged colored plates, with transparencies showing the motor points upon the surface of the body. We know of but one series of plates that are superior, and these are found in Mosher's *Electrodiagnosis*, where nerve and muscle groups are classified by means of colored

stars which represent the nerve points, and correspondingly colored circles which signify the muscles supplied.

The section on electrotherapeutics contains most of the new matter. Of the two types of static machine, the Wimshurst is preferred, this is not the machine of choice in this country. The uses of the static current are considered under the headings of breeze, head-douche, air-bath and sparks (*a*) as a means of massage, etc., (*b*) Morton's static induction current and wave current. The high frequency current has grown but little in favor since the preceding edition.

The final chapter considers the newer forms of current and of these the only one that has so far come into general practice is the sinusoidal current; this, with its modifications, the author regards as physiologically like the faradic current, though milder and a little less painful.

The slowly spreading use of Leduc's rhythmically interrupted galvanic current, and the condensation discharge, Cohn deploras, and says "both currents shall certainly be called upon in the future to play an important role in electric medicine." The only American physician whom we see mentioned is W. J. Morton.

This little work is written by an acknowledged authority, and its usefulness is shown by its having appeared in four languages, together with the call for this fourth edition. N. S. Y.

COMPENDIUM OF REGIONAL DIAGNOSIS IN AFFECTIONS OF THE BRAIN AND SPINAL CORD. A CONCISE INTRODUCTION TO THE PRINCIPLES OF CLINICAL LOCALIZATION IN DISEASES AND INJURIES OF THE CENTRAL NERVOUS SYSTEM. By ROBERT BING, Privat-Dozent for Neurology in the University of Basle. Translated by F. S. ARNOLD, B.A., M.B., B.Ch. (Oxon). Revised by DAVID I. WOLFSTEIN. Pp. 215; 70 illustrations. New York: Rebman Company, 1911.

It is indeed a pleasure to review this book, for the original in German is very well known to neurologists. The translation and revision has been well done and is fully up to the original.

This work is unquestionably the best small work on neurology printed in any language. It contains the essence or groundwork of neurology, and has the exceptional merit of being well and clearly put forth, so that the reader has no doubt as to the author's meaning. Besides, the illustrations are splendid and have that rare qualification, that is, they explain. It is distinctly the best work on organic neurology for students and general practitioners.

T. H. W.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF
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Functional Diagnosis of the Liver.—F. FALK AND P. SAXL (*Zeitsch. f. klin. Med.*, 1911, lxxiii, 325) publish their second communication on functional liver diagnosis. For purposes of study they have divided affections of the liver into four groups. Group I includes tumors of the liver like cancer, sarcoma, ecchinococcus, amyloid liver, leukemia, and chronic passive congestion. The parenchyma is affected secondarily. In Group II they place all infections and intoxications (typhoid, pneumonia, tuberculosis, chloroform, alcohol, phosphorus, for example). The third group contains those conditions in which the liver may be pathologically affected by the escape of bile from its normal passages (icterus from gallstones, from complete closure of the common duct, and from catarrhal conditions). In Group IV are placed the atrophic and hypertrophic cirrhoses of the liver. As functional tests, Falk and Saxl employed only those of known value, *i. e.*, levulose, urobilin, and the nitrogenous bodies—amino-acids, polypeptids, ammonia. Each of these tests was applied to their cases. The analysis of their results and of those reported in literature shows that a marked disturbance of liver function is disclosed, particularly in cirrhosis of the liver. Nitrogen ratios, urobilin excretion, and tolerance for levulose all reveal abnormalities. Such constancy of findings is seen in no other hepatic disease. In Falk and Saxl's cases these disturbances of function appeared early in the course of the disease. Often it was possible, by finding urobilinuria, levulosuria, and especially abnormal nitrogenous ratios, to arrive at the correct diagnosis at a stage of the affection when only vague gastric symptoms were present. In the remaining three groups the findings were less useful in a diagnostic way.

On Apical Rales.—KÜLBS (*Zeitsch. f. klin. Med.*, 1911, lxxiii, 169) has observed a number of patients with symptoms and signs suggesting pulmonary tuberculosis, which proved to be non-tuberculous. The symptoms complained of were shortness of breath on exertion, anorexia, and lassitude. Objectively, it was observed that the nutrition of the patients was only fair, excepting a few adipose individuals. The temperature remained normal. The examination of the internal organs revealed nothing unusual with the exception of the lungs. Here there was almost constantly a roughened (at times a diminished) vesicular breathing with prolonged expiration, usually heard over the right apex posteriorly, seldom over the left apex posteriorly or over the right anteriorly. In addition to these changes, medium-sized moist or dry rales were audible quite constantly in the same regions. The expansion was diminished, but without unilateral decrease. Röntgenographic study gave normal apices, not a sign of infiltration being found. In the cases subjected to tuberculin a positive reaction was not obtained. In one-half of the cases a mucoid sputum was expectorated; in all of these (11 cases) repeated examinations failed to reveal the tubercle bacillus. The patients were all young (under thirty-five years of age). Examination of the throat often showed a chronic pharyngitis, laryngitis, and tracheitis. With the subsidence of the latter, the pulmonary signs, which the author interprets as evidences of a chronic, non-tuberculous bronchitis, usually subsided or entirely disappeared.

The Destruction of Hemoglobin in the Liver.—L. HESS and P. SAXL (*Deutsch. Arch. f. klin. Med.*, 1911, civ, 1) have previously shown that the livers of white rats and rabbits, when subjected to aseptic autolysis, destroy their own hemoglobin so completely within a few days that the absorption spectrum of oxyhemoglobin entirely disappears. On the other hand, livers from animals that had been poisoned with yellow phosphorus, arsenic, strychnine, caffeine, chloroform, morphine, diphtheria toxin, adrenalin, pilocarpin, and strophanthin exhibited a marked retardation and diminution in their power to destroy hemoglobin. Such livers remained deep red for weeks, and quantitative determinations of hemoglobin showed a very slow reduction in quantity. Of the poisons enumerated, arsenic, phosphorus, chloroform, diphtheria toxin, and adrenalin are known to produce anatomical lesions in the liver, while strychnine and morphine are rendered non-toxic in the same organ. Caffeine may cause a glycosuria, but is otherwise without known effect on the liver. Since all the substances had the same effect on autolysis of the liver, Hess and Saxl believed they were dealing with an elective disturbance of the function of destroying hemoglobin. This supposition was the more likely, since the postmortem addition of these compounds was without any effect upon hemoglobin destruction. These studies led to similar observations on the human liver, in an effort to learn more of the pathology of hemoglobin destruction. Livers were obtained as soon as possible after death, and subjected to aseptic autolysis. Hess and Saxl found that the hemoglobin was completely destroyed within ten to twenty-five days in pulmonary tuberculosis (3 cases), scarlet fever (1 case), pneumonia (2), incarcerated hernia (1), cholera infantum (2), sepsis (2), measles,

leukemia, typhoid fever, diphtheria, phlegmon, meningitis, capillary bronchitis, erysipelas, and brown atrophy of the liver with cancer (each 1 case). On the contrary, there was slight destruction or none in pneumonia (5 cases), vitium cordis (2), gastro-enteritis (2), cancer of the liver (2), pulmonary tuberculosis (1), hereditary lues (2), measles, liver abscess, scolicoïditis, otitis media, cancer of esophagus, endocarditis, tuberculous meningitis, arteriosclerosis, scarlatina, diphtheria, lysol poisoning, and cirrhosis (1 case each). The inconstancy of the results Hess and Saxl attribute to the supposition that, as in the case of drugs, functional disturbance may be produced without anatomical lesions, and that a given disease does not affect the liver to the same degree in each instance. Reviewing the literature and analyzing their own material, Hess and Saxl show that with anatomical or functional disturbances of the liver, a polycythemia is at times observed, a result which one would anticipate if the hemoglobin destruction were diminished below the normal. Finally, to bring forth more evidence, Hess and Saxl served as experimental persons, and, after establishing their normal blood counts, observed the effect of various drugs on the number of their erythrocytes. The observations extended throughout a year. A marked increase, up to 7,000,000 was found after tincture of opium. Definite but less striking figures are reported following Fowler's solution, caffeine, strophanthus, and cognac. The increase in cells was gradual, reaching its maximum in ten to fourteen days. These results are interpreted as evidence of the inhibitory action of the above-named drugs upon the hemoglobin-destroying function of the liver.

The Adrenalin Content of the Adrenal Glands.—A. INGIER and G. SCHMORL (*Deutsch. Arch. f. klin. Med.*, 1911, civ, 125) have made quantitative determinations of the adrenalin in the adrenal glands in a series of 517 cases. Their exhaustive study adds much valuable information to a field which is none too well illuminated. Their observations cover such a wide range of material that it is possible to indicate the results only by quoting their summary: (1) In the examination of 517 patients at autopsy, the average adrenalin content of both adrenals was 4.22 mg. Up to the age of nine years the adrenalin averaged 1.52 mg.; between ten and eighty-nine years the average was 4.59 mg. (2) During the first few years of life the adrenalin content gradually increases, but from the tenth year onward there is little variation. (3) In the diseases studied, the adrenalin varied within relatively narrow limits. (4) In the infectious diseases, a decrease of adrenalin was not demonstrable as a rule. (5) In atherosclerosis, the amount of adrenalin was only slightly augmented. (6) In acute nephritis, contracted kidney (including chronic nephritis), and in chronic cardiac diseases, an increase beyond the average adrenalin content was demonstrable. (7) In Addison's disease the adrenalin in the adrenal glands was nil. (8) Diabetes gave a somewhat diminished quantity of adrenalin. (9) In status thymolymphticus a slight decrease was seen in the majority of the cases; sudden death in this condition cannot, however, be attributed to an exhaustion of the chromaffin system. (10) In cases of sudden death (as from violence) an increased quantity of adrenalin was observed in most instances, but not with sufficient constancy to give diagnostic value to the finding. (11) When death followed within twenty-four hours after

narcosis, the amount of adrenalin was somewhat subnormal. (12) When death followed convulsive seizures, the quantity of adrenalin was also below the normal. For the quantitative determinations of adrenalin, Ingier and Schmorl modified Comesatti's method, using adrenalin (Takamine) solutions as standards. Histological examinations of the chromaffin tissue were also made.

The Bacteriology of the Cockroach.—C. CONYERS MORRELL (*Brit. Med. Jour.*, London, 1911, ii, 1531) describes the life history of cockroaches, their method of feeding and growth, and then mentions experiments conducted bacteriologically. Animals were kept aseptically until defecation occurred, then cultures were made from the feces, with resulting growth of *Bacillus lactis aërogenes*, *Bacillus cloacæ*, and moulds of the *Aspergillus* variety. In order to prove the transmission of known organisms, animals were fed tubercular sputum, pus containing staphylococci, and aspergillus spores. Tubercle bacilli (identified by staining reaction) were present in the feces passed within twenty-four hours of feeding. Cultures of both organisms and mould were obtained from the feces of the pus and spore-fed animals. Morrell concludes that the common cockroach is able, by contamination with feces, to bring about the souring of milk, to infect food and milk with pathogenic organisms, and thus possibly to become a dangerous domestic pest.

A Cutaneous Reaction in Syphilis.—HIDEYO NOGUCHI (*Jour. Exper. Med.*, 1911, xiv, 557) has prepared from pure cultures of *Treponema pallidum*, a substance analogous to tuberculin, to which he has given the name "luetin." The spirochetes are grown at 37° C. for periods of six, twelve, twenty-four, and fifty days, anaërobically, on a medium of ascitic fluid, or ascitic fluid agar containing placenta. The agar cultures thus obtained were ground, and the resulting thick paste was gradually diluted, until the emulsion became liquid. This preparation was heated to 60° C. for an hour, and 5 per cent. carbolic acid added. When examined microscopically, 40 to 100 dead pallida were found per field, cultures from which showed no growth. A similar emulsion with uninoculated medium was used for control. "Luetin" was tested experimentally, with the observations that repeated inoculations of either living or killed pallida into testicles of rabbits lead to a condition in which an intradermic injection of luetin in dosage of 0.05 c.c. was followed by a well-marked cutaneous reaction. A corresponding reaction was not obtained in normal animals, in those suffering from active syphilitic orchitis, or in those in which the condition had been cured by the administration of salvarsan four months previously. Luetin was tested similarly on 177 syphilitic cases; 77 parasyphilitic, and 146 control patients. No marked constitutional effect was noted beyond slight fever or malaise. Control cases showed no reaction. In positive cases the reaction was: (1) Papular, appearing in twenty-four to forty-eight hours, developing induration lasting about a week. (2) Pustular, at first resembling the former, but after four or five days progressing to pus formation. (3) Torpid form, resembling negative cases, but suddenly after ten days or more lighting up. The analysis of the human cases showed that in cases of primary or secondary syphilis, which had had either insufficient treatment or none at all, no

skin reaction occurred except in a few instances. In the positive cases the reaction was always papular. On the other hand, most secondary cases which had been mercurialized before the administration of salvarsan, or which had remained without symptoms for some months after salvarsan injections, gave striking and unmistakable reactions. The reactions in tertiary or hereditary syphilis were the most intense, and appeared more constantly than the Wassermann reaction. On the other hand, syphilis of the central nervous system reacted positively to luetin, less constantly than to the Wassermann. Among cases treated with salvarsan, two groups gave negative or doubtful reactions, the one doubtful, in those cases without symptoms, but with the reappearance of the Wassermann reaction; the other always negative, in cases that remained without clinical symptoms or Wassermann reaction for many months. In conclusion Noguchi states that it remains to be determined in how far the cutaneous reaction can be used to supplement the Wassermann test in determining the complete and permanent suppression of syphilitic infection; it appears probable, however, that the Wassermann is more constant in primary and secondary disease; the cutaneous in tertiary and latent syphilis.

The Experimental Production of Appendicitis by the Intravenous Injection of the Diplococcus.—F. J. POYNTON and ALEXANDER PAINE (*Proc. Roy. Soc. Med.*, London, 1911, v, Path. Sect., p. 18,) describe experiments with a culture of a diplococcus obtained from the knee-joint of a boy with acute articular rheumatism, who later, under salicylate of soda, made complete recovery. Twenty-four young rabbits were inoculated intravenously in varying doses, either with the original or subcultures. Of these, 4 developed, in addition to arthritis and mucous diarrhea, an acute appendicitis of varying severity, involving the outer half of the appendix. Histologically, transitions were found from the earliest stage of infection by the blood stream, with the first changes appearing in the mucous and submucous coats, to complete destruction of normal tissue, ending either in necrosis, minute ulcer formation, or the early connective tissue proliferation of healing. Diplococci were visible within phagocytes. In one case early manifestations of general peritonitis were present with living organisms in the peritoneal fluid, yet without signs of perforation. In another, there was a ballooning of the affected area, suggesting the possibility that in man some such loss of tone may favor the stagnation of secretions and contents, with resulting concretion formation. In no cases were there other visceral lesions. Ten years ago, Adrian reported similar cases of experimental appendicitis in rabbits, produced by the intravenous injection of streptococci, staphylococci, pneumococci, typhoid, and colon bacilli. He does not mention the source of the organisms used nor describe any ulcer formation, or accompanying lesion such as arthritis. He reviews the literature of the subject. Poynton and Paine conclude that the histology of these and many human cases are very similar. The association of arthritis, mucous diarrhea and appendicitis is interesting, in its bearing on auto-intoxication from the bowel as a cause of arthritis. These observations make it seem possible that all lesions may be the result of a primary cause circulating in the blood stream and determining to these various positions.

SURGERY

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The Choice of the Method of Exposing the Heart for Suture.—KÖNIG (*Deutsch. Zeitsch. f. Chir.*, 1911, cxii, 490) says that it is desirable, in exposing the heart for suture, not only to employ a typical method, but to have regard for the special circumstances of the particular case. When there is a penetrating wound to the right of the sternum, a sternal method should be used without exception. All methods which remove a part of the sternum only are time consuming and not easily performed, so that they are dangerous and to be avoided as much as possible. Extrapleural methods, where the pleura is intact, are to be unconditionally preferred, but where the pleura is already wounded, the transpleural method is to be preferred, if no time is to be lost by it. The approach to the heart must be as wide as possible, the disturbance in the firmness of the thorax as slight as possible. The method which provides these requirements best is the Kocher, especially for wounds between the left sternal border and the mammary line. The horizontal portion of the incision passes from the left chondral junction along the cartilage (second to fourth, according to the necessity), the vertical portion along the middle of the sternum, and the oblique portion along the sixth costal cartilage, the included cartilages being resected. When the heart wound is external to the mammary line, the Rotter flap is to be preferred, because by it a direct canal can be followed to the wound in the heart. This flap has its base at the left border of the sternum, is rectangular, extends outward to beyond the mammary line, and from the third to the fifth rib.

Recurrence of Ulcer of the Stomach after Gastro-enterostomy.—FINK (*Zentralbl. f. Chir.*, 1911, xxxviii, 1497), on November 16, 1908, did a posterior gastro-enterostomy on a man, aged forty-three years, in whom he found an ulcer involving the anterior and posterior walls and lesser curvature; and these were adherent to the liver. The ulcer had a characteristic appearance and was associated with a considerable dilatation of the stomach. After the gastro-enterostomy the symptoms disappeared, the patient gained strength and put on weight. He returned to work, looked well, and could take all kinds of food without care or choice. This condition lasted two years. For four weeks

he had been suffering from marked symptoms of ulcer, with severe bloody vomiting on two occasions, and marked loss of weight, when, on December 29, 1910, Fink again opened the abdomen. There was found at the same place as in the first operation a callous ulcer, which had incompletely occluded the pylorus and was associated with a slight dilatation of the stomach. At the site of the gastro-enterostomy, the jejunum was adherent to the stomach for not quite 10 cm. The communicating opening between the two could not be felt. The ulcer-bearing area in the pyloric region was removed for about 10 cm. and the stomach closed by direct apposition. On examination through the resection opening, the communicating aperture with the jejunum could not be seen. The healing after the second operation was uneventful, and the patient did well. Fink saw a causal relationship between the closure of the gastro-enterostomy opening and the recurrence of the ulcer. In the first place the passage of the stomach contents through the new opening relieved the ulcer of irritation, so that it slowly healed. The stenosing effect of the ulcer upon the pyloric opening being removed, this aperture gradually assumed its normal proportions, so that the food could again take its physiological course through the pylorus. The gastro-enterostomy opening then having no work to do, closed. The conditions favoring the reestablishment of the ulcer were again present. Its development with inflammation of the surrounding tissues brought about a relative pyloric stenosis and consecutive extension of the ulcer and hemorrhage. According to the evidence in this case, closure of the gastro-enterostomy opening is to be expected in every case of ulcer which, as it does not lie directly at or near the pylorus, gives rise to only a relative stenosis; so that after the ulcer has healed the stomach contents can be emptied in the normal manner. In these cases of ulcer recurrence after gastro-enterostomy Fink recommends the operation of excision of the ulcer.

The Importance of the Inhalation of Oxygen in Thoracic Surgery.—TIEGEL (*Zentralbl. f. Chir.*, 1911, xxxviii, 1529) says that in a previous communication he called attention to a simple and practical principle in thoracic surgery. The chief danger of an operative pneumothorax lies in the insufficient ventilation of the lung, and the resulting deficiency in oxygen. Tiegel says this can be best overcome by the inhalation of oxygen. A man may preserve a sufficient respiration, even with an open pneumothorax, so that he will do much better if oxygen is substituted for air. This will raise the depressed respiratory exchange fivefold. Animal experimentation demonstrates this by showing that the inhalation of oxygen under a minimal pressure (1 cm.), which does not distend the lung, gives a better arterialization of the blood than occurs with the usual differential pressure. Tiegel has employed this method in a number of cases, and has observed no disadvantages from it, even in long continued operations. There was no dyspnea or cyanosis during the operations on the collapsed lungs. This among many others was the most important technical advantage. The great superiority of the use of oxygen over the air pressure is shown by the following experiment: A young dog was given intravenously 5 mg. of a tuberculous culture (human type). Some months later the dog was very much emaciated, and exhibited marked dyspnea. Narcosis

was conducted under oxygen inhalation, whereupon the dyspnea was improved. An incision was made, and the blood found to be bright red. For economical reasons, a differential pressure with air of about 12 cm. (overpressure), was maintained. The lung, which showed high-grade tuberculous changes, remained filled and in close contact with the chest wall. Yet the breathing was dyspneic and the blood cyanotic. It was suspected that this was due to a closing of the glottis by a falling backward of the tongue or epiglottis, but this was disproved by the rhythmical movement of the gas bag. Because the dyspnea increased to the point of threatening suffocation, Tiegel, keeping up the same pressure, substituted oxygen for the air. Immediately the dyspnea improved and the blood became bright red. The dog died soon after the operation, and an examination showed an extensive tuberculosis of both lungs.

The Treatment of the Duodenal Stump in a Gastro-enterostomy by the Billroth II Method.—FÁYKISS (*Zentralbl. f. Chir.*, 1911, xxxviii, 1532) advises the following method of overcoming the difficulties associated with the closure of the duodenal stump: After careful closure of the stump by means of a suture including all the coats, he sutures the pancreas over it. When possible he includes in the suture the peritoneal covered portion of the duodenum, and if the stump is too short to permit this the posterior parietal peritoneum is employed. The fine intestinal needle must grasp the pancreas, superficially, and the great bloodvessels must be avoided. Finally, the covering of the stump by the pancreas must be complete. The operation works well also in those cases in which, with the tumor, a part of the pancreas must be removed. This happened in two cases in which the wounded surface of the pancreas was made to cover the duodenal stump. Fáykiss employed this method in 6 cases. It was successful in all, the healing being good and no fistula occurring.

Anesthesia by Intratracheal Insufflation.—COTTON and BOOTHBY (*Surg., Gyn., and Obstet.*, 1911, xiii, 572) say that the technical difficulties of intubing the trachea have prevented, in all but the most enthusiastic hands, the application of Meltzer and Auer's intratracheal insufflation anesthesia. Cotton and Boothby have devised an introducer, in curve and angle, following nearly the O'Dwyer intubing apparatus, in use being rather different. When the patient is etherized fully with inhaler or cone, a mouth gag is inserted on the patient's left, the tongue is dragged forward sharply with tongue forceps, the operator's left index finger is thrust down until it meets the epiglottis, and the "introducer," held in the right hand, is pushed in and down, alongside the left forefinger, till it has passed the upper projecting edge of the epiglottis. Then the heel of the instrument is pitched upward, and the assistant feeds the catheter into the larynx and trachea. The curved end of the "introducer" is tubed for the passage of the catheter through it, in order to prevent buckling of the rubber tube. At first nitrous oxide was given with the usual oxygen co-efficient till consciousness was lost, and anesthesia was then deepened by the addition of ether till the laryngeal reflex was abolished and when the intratracheal tube was introduced. No air was used, only nitrous-oxide-oxygen-ether.

Presently the ether was cut off, and the greater part of the operation was performed under nitrous oxide and oxygen alone. At no time was there the slightest trouble. A relative apnea was quickly established and continued (more or less completely) throughout. At the end of the operation the patient was "blown out" with pure oxygen as usual. So far as Cotton and Boothby know, the only gas-oxygen apparatus which it is safe to use for intratracheal work is the one which they have recently devised, for the details of which they refer to their other papers.

The Treatment of Perforated Duodenal Ulcers.—OFFENBERG (*Zentralbl. f. Chir.*, 1911, xxxviii, 1625) says that the treatment of a perforated duodenal ulcer cannot be uniform, but must depend upon the circumstances of the individual case. Whether it is to be sutured or a gastro-enterostomy done, depends not so much upon the anatomical relations of the markedly inflamed field of operation. He reports the case of a man, aged twenty-eight years, who suddenly during the night, was taken with a severe pain in the epigastrium. He has been previously well, and when attacked felt as if a knife had passed from the origin of the pain to the right lower abdominal region. On admission to the hospital, he exhibited the picture of a perforation peritonitis. Pressure in the ileocecal region produced as much pain as pressure in the epigastrium, so that an appendicitis was thought of. The operation was performed twelve hours after the occurrence of the perforation. There was found in the anterior wall of the duodenum, opposite the papilla of Vater, a round hole, out of which poured forth a well of bile and pancreatic fluid. The latter had already produced everywhere fat necrosis. At first an effort was made to suture the ulcer, but repeated efforts failed because of the fragility of the tissues. Since time was pressing, a posterior, retrocolic gastro-enterostomy was immediately performed. After cleansing the peritoneum, a tampon was pressed strongly against the ulcer opening to prevent the escape of the intestinal fluid. The liver was then pressed down on the ulcer and fixed in this position by gauze pressed in between the surface of the liver and the costal margin. The wound was closed in the usual way, and the usual precautions taken. The gauze tampons were gradually removed during the after-treatment. The patient left his bed fourteen days after the operation. The fear of a duodenal fistula was not realized. The liver pressed down on the ulcer opening, acted like a valve in closing it, and the liver was not separated from it after the removal of the tampons.

Substitution of the Esophagus by a Plastic Operation on the Stomach.—HIRSCH (*Zentralbl. f. Chir.*, 1911, xxxviii, 1561) says that while the technique of gastrostomy is so highly developed, much remains to be desired, even in successful cases, and we ought to aim at a plastic substitution of the esophagus that will permit the patient to introduce the food by his mouth. Roux accomplished this purpose by using a resected piece of the jejunum, but this has obviously many disadvantages. Hirsch proposes to make an esophagus from a flap taken from the anterior wall of the stomach. The abdomen is opened by an incision from the sternum to the umbilicus. The stomach is drawn out as far

as possible, and from the anterior wall is made a long rectangular flap, consisting of the whole thickness of the wall, with its base above turned as much as possible toward the lesser curvature to provide the best nourishment (the vessels of the anterior wall come chiefly from the lesser curvature). This flap is turned upward, and the defect in the stomach closed by layer suture. This suture is continued upward without interruption to the flap, which is sutured around a tube to form the new esophagus. The stomach is returned into the abdomen, and the abdominal wall closed. The junction of the new esophagus with the stomach is sutured to the upper end of the abdominal wound by the peritoneal suture, which was left long for the purpose. This prevents at this point a kinking of the esophagus as it is coming out of the abdomen. It is then conducted under the skin of the thorax, and its upper end fixed as high as possible, so that at a later operation it can be made to communicate with the normal esophagus. Experiments on the cadaver showed that the flap from the normal stomach can be brought up easily to the neck. If the stomach cannot be drawn out of the abdomen, the operation cannot be done. The study of injected specimens from the cadaver showed that there were always several branches of the left superior gastric artery which entered the flap and continued to its end. In operations on dogs the flaps were preserved. Physiology teaches that in swallowing the mass of food passes to the stomach in less than a tenth of a second—*i. e.*, before the contraction of the pharyngeal and esophageal muscles occurs. This contraction follows the act of swallowing and forces down only the remains of the swallowed mass or large masses. Hirsch has not yet had an opportunity to perform the operation on the human as the indications are limited and the cases, therefore, few. He thinks that the principle can be applied to other hollow organs, as in the substitution from the bladder of a portion of the ureter or the urethra.

A New Manipulation during Narcosis.—GONTERMAN (*Zentralbl. f. Chir.*, 1911, xxxviii, 1626) says that to the indispensable implements for anesthetization belong the mouth gag and tongue forceps. What unpleasant sensations are left after the use of the tongue forceps are well known, as are the complaints of the patient concerning pain at the angle of the jaw from the use of the mouth gag. Gonterman substitutes for both the following method of accomplishing the same purposes: With the head in the low position, after opening the mouth with the gag, a broad, round, gauze pad, 3 to 4 cm. thick, held on a handle, is introduced on the side of the mouth opposite the gag. In order that the tongue already, fallen back, may not be forced further back, and at the same time that it may be lifted forward and later held there, it is desirable that the introduction of the pad with the handle holding it, should be made with a rotating movement, so performed that the tongue is lifted forward. The pad is then rolled on the surface of the tongue until it rests on the base in front of the epiglottis, when the tongue will be resting on it. By pressing it forward in the direction of the submental region not toward the opening of the mouth, which would allow it to slide off, the tongue is lifted forward. The epiglottis follows this movement, and the larynx is kept open. It is easy to hold the instrument in this way during the whole operation, but it is ren-

dered more easy by resting the shaft of the handle on the upper teeth. Since the pad gradually becomes saturated with mucus, it must be changed from time to time. After the introduction of the pad and handle the mouth gag is no longer necessary and should be removed. The laying on of the mask for anesthesia is only slightly influenced by this method. Gonterman has employed it in many cases, in some lasting several hours, and has found it very satisfactory.

THERAPEUTICS

UNDER THE CHARGE OF

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The Indications of Treatment with Lime-poor Food.—HIRSCHBERG (*Berlin. klin. Woch.*, 1911, xlviii, 2056) says that it has been proved that there is an abnormal amount of lime salts in the articular cartilages in cases of arthritis deformans. Schüller has had favorable results in the treatment of arthritis deformans by limiting the amount of lime in the diet, and Hirschberg substantiates his results by similar effects obtained by him in the treatment of this disease and other forms of arthritis. Hirschberg puts these patients on a test diet with an approximate lime content expressed as CaO of 1.86 grams. If no more than 10 per cent. of this lime is eliminated in the urine he considers that there must be retention of lime. The diet is then changed to one poor in lime, and these patients are kept on this lime-poor diet for six to eight weeks. The chief articles to be avoided in a lime-poor diet are milk, butter, yolk of eggs, potatoes, and spinach. Other vegetables are given in small amounts, and distilled water only should be allowed with the diet. Hirschberg found that a marked improvement was obtained in many severe joint affections, as measured by both subjective and objective symptoms. This improvement was especially notable in cases with marked ankylosis of the spine of the Bechterew and Strümpell-Marie variety. Likewise, notable benefit was observed in cases of arthritis deformans and in joint pains following acute attacks of multiple joint inflammation.

Creatin and Creatinin in Animal Metabolism.—THOMPSON and WALLACE (*Brit. Med. Jour.*, 1911, 2652, 1065) believe that the retention of creatin, whether given with food or formed in the body, is intimately connected with carbohydrate metabolism. They found that the excretion of creatin in the urine apparently bore a direct relation to the severity of the glycosuria in 3 cases of diabetes. The addition of creatin in doses of 1 grain to the diet of the mildest case had no appreciable effect on the output of sugar. Coincidentally there was a marked diminution in the excretion of creatinin in these cases

of diabetes that showed the increase of creatin excretion. The administration of creatinin in doses of 0.15 to 0.18 gram, either given hypodermically or with the food, temporarily increased the excretion of sugar nearly 50 per cent. From this they raise the practical point that soups, meats, and meat extracts rich in creatinin should be excluded from the diabetic diet.

The Physiological Action of Amorphous Digitoxin-digalen.—SYMES (*British Med. Jour.*, 1911, 2655, 1346) relates animal experiments regarding the physiological action of digalen that seem to support the conclusions that digalen is an active preparation of digitalis producing characteristic effects on the circulatory system and on the secretion of urine. Intravenous, subcutaneous, and intramuscular injections have produced no local trouble. Symes believes that the human subject in immediate need of digitalis will react more satisfactorily to the administration of the drug intravenously.

The Treatment of Amebic Dysentery.—ANDRESEN (*Med. Rec.*, 1911, lxxx, 1024) believes that the ipecac treatment of amebic dysentery is by far the best method. This method of treatment has been in use in India for many years, and is now the accepted method of treating amebic dysentery in the Philippine Islands. He gives the details of the treatment, for he believes that close attention to details is necessary to secure the best results. The patient is best put upon a liquid diet or a light diet leaving only slight residue. An initial dose of castor oil is administered, and cold enemata are given twice a day. The cold enemata may be a saline solution; quinine solution, 1 to 500; or thymol, 1 to 2000. These enemata relieve tenesmus and wash out debris, but it is almost certain that local antiseptics have no effect upon the amebæ in the colon. The ipecac is best given in 5-grain salol- or keratin-coated pills. A pill larger than 5 grains is very difficult to swallow, and may not readily pass the pylorus. Ipecac is best given about eight o'clock in the evening, and no food should be given for four hours before the treatment is begun. It is usual to give about 20 minims of tincture of opium a short time before the ipecac is to be given. The initial dose of ipecac should be large, Simon recommending as much as 40 or 60 grains. Andresen has found that excellent results were obtained with an initial dose of 30 or 40 grains. If the pills are properly coated, the patients frequently do not vomit at all. If they do vomit, the vomitus usually consists of a small amount of clear mucus. If vomiting is more marked and distressing, it may be controlled by application of ice-bags to the throat, mustard paste to the epigastrium, or by hypodermic injections of morphine. The dose is reduced 5 grains every evening until the dose has reached 10 grains, and this dose is continued for two weeks. The smaller doses often give rise to more nausea and vomiting than do the large initial doses, and it may be necessary to decrease the dose still further until a point of tolerance is reached. This dose is then continued for about two weeks, even though there are no active symptoms of the disease. Andresen says that, under this form of treatment, the diarrhea stops within a day or two, and scrapings made from the rectum as early as forty-eight hours after the first dose fail to reveal the amebæ. The ulcers

frequently heal in less than a week. The first week or ten days of the treatment should be spent in bed. After the first two or three weeks of treatment a more liberal diet is allowed, but the return to a normal diet should be gradual. When the treatment has been thoroughly carried out, complications are rare, and return of the condition after months or years is much less common than after other methods of treatment.

The Diagnosis of Gout by Therapeutic Test with Atophan.—ZUELZER (*Berlin. klin. Woch.*, 1911, xlvii, 2101) has observed that the increased elimination of uric acid in gouty subjects after the use of atophan is associated with a marked diminution in the uric acid content of the blood. This increased elimination of uric acid and diminished uric acid content of the blood go hand in hand with a marked improvement in the clinical symptoms. Weintraud and others have found that uric acid injected intravenously into gouty patients is rapidly excreted when atophan is given at the same time, while, on the other hand, if atophan is not given, gouty individuals retain the injected uric acid for a long time. They have also found that the same increase of uric acid excretion occurred when the sodium salt of nucleic acid was given with a simultaneous dose of atophan. They believe that the chief etiological factor in gout is an inability of the kidney to excrete uric acid. They explain the action of atophan in gout by a direct and selective stimulating action of atophan upon the kidney that increases its ability to excrete the uric acid. Zuelzer does not believe that this explanation is sufficient, although it may be partially true. He believes that the increased elimination of uric acid in gouty subjects following administration of atophan is of diagnostic value in differentiating true gouty affections from non-gouty joint inflammations. He says that the urine of a true case of gout under treatment with atophan will show an abundant urate deposit sufficient to be recognized by the gross appearance of the urine. This deposit of urates will not occur in non-gouty patients. There are, of course, exceptions to this general rule, but Zuelzer believes that this rough test will differentiate the majority of cases of true gout. He adds a note regarding the good results obtained by him in the treatment of recent cases of neuralgia with atophan.

Recovery of a Typhoid Bacillus Carrier during Vaccine Treatment.—BREM and WATSON (*Arch. Int. Med.*, 1911, viii, 630) review the literature of the treatment of typhoid bacillus carriers. Eleven recoveries have occurred, and 5 of these patients recovered during vaccination with autogenous vaccines. Brem and Watson report the case of a child from whose urine typhoid organisms in pure culture were isolated one month after her discharge from hospital. The child was treated with autogenous vaccines, nine doses in all being given with an initial dose of 25,000,000, gradually increased to 1,500,000,000. Eleven successive urine cultures were positive during the period of treatment, that continued six months after the acute symptoms of the attack of typhoid fever. During the next three months five successive cultures were negative for typhoid bacilli.

The Treatment of Pernicious Anemia with Intramuscular Injections of Defibrinated Blood.—ESCH (*Deutsch. med. Woch.*, 1911, xxxvii, 1943) reports a case of pernicious anemia with a red blood count of 448,000, and a hemoglobin percentage of 22, successfully treated with intramuscular injections of defibrinated blood. He injected 35 c.c. of defibrinated blood taken from a woman whose blood showed 70 per cent. of hemoglobin. Dyspnea, nausea, and vomiting ceased after the first injection, and there was a considerable improvement in the general condition of the patient. Three more injections were given in the course of two weeks, and at the end of this time the hemoglobin had risen to 53 per cent. Five injections were given in all, in amounts of from 25 to 70 c.c., and at the end of two months the hemoglobin percentage was 75, with no subjective symptoms of the disease.

Salvarsan.—EHRlich (*Münch. med. Woch.*, 1911, lviii, 2481) gives a brief review of some of the more important articles on salvarsan therapy. He says that the consensus of opinion is that salvarsan is a relatively harmless drug. A number of fatalities ascribed to salvarsan have been shown to be due to entirely different causes. The fever and constitutional symptoms at first attributed to salvarsan are due to the use of old distilled water, and they may be avoided by using water freshly distilled to make up the salvarsan solution. Ehrlich says that salvarsan therapy has simply brought into prominence the subject of nerve recurrences, and these have been falsely cited as evidences of salvarsan poisoning. He says that a close study of reports of cases treated with mercury has shown that nerve recurrences are more common after treatment with mercury than after salvarsan therapy. Ehrlich advises the combined treatment of syphilis by giving the salvarsan in a large dose and following it up with active mercurial treatment by means of intramuscular injections. The list of diseases favorably influenced by salvarsan therapy is a large one, and Ehrlich names those in which it exerts a more or less specific action. This list mainly comprises those diseases that are caused by some form of spirillum. Among these are fowl spirillosis, recurrent fever, yaws, tertian malaria, Aleppo boil, bilharzia, pneumonic plague of horses and African farcy. Ehrlich does not believe that it is possible to improve upon salvarsan, since this remedy was the result of long experimentation, as its former name "606" implies.

The Therapeutic Use of Iodine in Nascent State.—KAUFMAN (*Berlin. klin. Woch.*, 1911, xlviii, 2251) has had good results in treating various local conditions by the application of a potassium iodide solution that is followed by the use of a solution of hydrogen peroxide. He says that iodine is set free from the iodide solution in its nascent state by this method. The amount of iodine set free is controlled by the strength of the solution used. Thus he uses from very dilute solutions of the iodide up to the maximum limit of a 5 per cent. solution, and the hydrogen peroxide solution in varying strengths from 0.1 to 1 per cent. A solution of sodium perborate with the addition of a small amount of citric acid may be used in place of the hydrogen peroxide solution. He claims that this method is very efficacious in various catarrhal affections of mucous membranes, particularly in subacute or chronic urethritis.

PEDIATRICS

UNDER THE CHARGE OF

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Colon Irrigation: The Short vs. the Long Tube.—HENRY T. MASCHELL (*Archiv. f. Pediatrics*, 1911, xxviii, 837) prefers the short rectal nozzle to the rubber catheter in giving colon irrigations to children. Some of the objections to the rubber catheter are that it often kinks, shutting off the flow; that it curls on itself, and the tip appears at the anus; that it causes more irritation and discomfort, since it must be introduced by a series of pushes or shoves, and that traumatism to the mucous membrane is possible if the catheter is stiff or carelessly inserted. The small nozzle, on the other hand, is easily inserted, and gives a minimum of anal irritation. It is also practically safe to be used by untrained attendants. Maschell gives an analysis of 200 consecutive irrigations on infants, comparing the short nozzle and the rubber catheter alternately. The analysis shows that for the "amount injected" the short nozzle had the advantage, and that it was retained for a longer time with the short nozzle. The fluid can be made to reach the cecum by using the short nozzle, and the irritation and discomfort is less than with the catheter.

The Physiological Significance of Calcium Deficiency in Breast-fed Infants in the First Year.—W. DIBBELT (*Berlin. klin. Woch.*, 1911, xlviii, 2062) determined the amount of calcium necessary to each 100 grams increase in body weight, and applying this to Cammerer's table for the rate of body growth, formulated the amount of calcium necessary for each month of life during the first year. He then compared this table with one showing the amount of calcium the child derives normally from the mother's milk per month and found that for the first six months of life there is a marked difference between the supply and demand of calcium. For instance, in the first month the demand is 0.3246 grams, and the supply through the mother's milk is 0.1512 grams. Aron and Schabad, making similar observations, place the percentages slightly larger than Dibbelt, but show the same difference in supply and demand for the first six months of life. It must also be considered that a calcium content of 0.05 per cent. in mother's milk, upon which these tables are based, is often not reached, and the calcium content may be very much lower. During the earlier months of life there occurs in the skeleton, and especially in the long bones, a porosis, or absorption, and the calcium contents of the bony system becomes reduced. That this is a physiological process was apparently proved by Thomas in a number of experiments on puppies and kittens. He found the same reduction in the ash-content in these animals at the corresponding age period. Comparing the results from animal and human investigation, Dibbelt concludes that in all suckling animals,

from birth to the first doubling-period of weight, the body and the skeletal system develop under the influence of a calcium deficiency. The process of absorption of bone occurring after birth which enlarges the marrow-space and makes room for the red bone-marrow, is accompanied by a certain loss of calcium. At this period a nourishment poor in calcium salts would tend to assist this process of bone absorption. Herein Dibbelt sees the physiological significance of calcium deficiency in the first six months of life, which makes possible and encourages the natural process of bone absorption taking place at this period. The pathological significance in this relation appears when the calcium deficiency of a nourishment for the first six months falls too far below the determined necessary 0.04 or 0.05 per cent. Seemann and Pfeiffer's analyses of the milk of mothers whose infants were rachitic show a calcium content varying from 0.029 per cent. to 0.019 per cent., and 0.17 per cent. instead of the required 0.04 to 0.05 per cent. Dibbelt produced disturbances of the calcium content in the bones of suckling puppies which gave clinical symptoms similar to those of beginning rickets by feeding the dam with a diet almost free from calcium. The end of the first six months of life marks a period of lowered skeletal resistance. The attendant calcium deficiency in the nourishment may predispose to a subsequent condition of rickets. The establishment of rickets in the first year of life is associated with the influence the calcium salts exert on the child's body and skeletal system.

Clinical and Bacteriological Observations on Influenza in Infants.—ERICH MÜLLER and ERICH SELIGMANN (*Berlin. klin. Woch.*, 1911, xxxvi, 1636) report the clinical and bacteriological findings on a large number of cases of influenza in infants. Only the unusual forms of this disease are discussed. Two forms are particularly mentioned: One, in which a clinical picture of sepsis is developed; the other, in which there are suddenly developed formations of exudate in the serous cavities of the body. The septic type is characterized by very sudden intermissions of temperature and variations between 40° C. and 37° C. No organic lesions can be demonstrated, and the general condition of the child is not, as a rule, seriously affected. While many of these cases recover completely within a few days, other cases are seen which either become prostrated at the onset, or, after repeated relapses, sink after weeks into a septic condition and die, without even the autopsy showing any special organic lesion. A further danger of this type of cases is the possibility of infecting other children, since such cases are often prolonged throughout the summer with their varying periods of normal temperature. Among the types exhibiting the formation of an exudate, that affecting the pleura in the form of an empyema is relatively frequent. The empyema may develop at the onset or after several days. The prognosis is usually bad, especially with rib resection, etc. A minimum of shock, with just enough incision to relieve the pressure somewhat, and a gradual drainage have given the best results in these cases. Still more hopeless are cases in which the exudate occurs in the peritoneal cavity. Here also the localizing signs may develop immediately, simulating a primary peritonitis; or, after several days of indefinite illness, the peritoneal symptoms set in with a sudden rise in the temperature. Distention of

the abdomen is the first ominous sign, and the superficial veins on the abdomen are prominent. The course of the disease is here rapidly fatal, with septic symptoms. The bowel movements are normal or slightly dyspeptic, and vomiting, while it occurs, is not a prominent symptom. Convulsions occur in the later stages. Autopsy shows a purulent exudate with marked formation of fibrin. A local cause for the condition was not found in these cases, the appendix in particular being intact. The infection, therefore, occurs directly from the bowel or, more probably, through the blood stream. Müller and Seligmann report a number of cases showing cerebral symptoms, with bulging fontanelle and convulsions. Lumbar puncture indicated a serous meningitis, with high pressure and a sterile fluid, and the autopsy verified this, although the process had not formed an exudate, which might easily occur in subsequent epidemics. Besides the influenza, bacillus of Pfeiffer, which does not play the chief role in the influenza of infancy, many other organisms have been found as etiological factors, especially pneumococci (Esherich) and diplobacilli (Trumpp). This being the case, the disease known as "grippe" clinically combines a number of different infectious diseases, from an etiological standpoint. In this epidemic referred to by Müller and Seligmann cultures from the throat (50) showed regularly diplococci and streptococci, which, however, were not characteristic when cultured. Influenza bacilli, diplobacilli, and pneumococci were routinely absent. However, a microorganism was isolated twice from discharging empyemas. This coccus showed individual characteristics, differed culturally from the ordinary cocci, and was subsequently found routinely in the blood and organs of children dying from grippe. The identical coccus was found in 8 different cases. In the blood after death these cocci are small and occur singly, or attached by twos or threes. Chains of more than five or six were never seen. These are found also in septic conditions and in cases with exudate. The same organism is found regularly in the lung tissue, in the spleen, and occasionally in other large organs. Lumbar puncture was sterile. This microorganism seems to be a coccus belonging to the group of streptococci, but differing from them culturally to such a degree that Müller and Seligmann accept it as the causal organism of that epidemic and call it the grippe-streptococcus.

A Case of Amyotrophic Lateral Sclerosis in Childhood.—BOLDT (*Med. Klinik*, 1911, vii, 1773) reports a case of amyotrophic lateral sclerosis occurring in an otherwise healthy boy aged eight years. This disease is very rare in childhood, occurring usually in middle-aged persons. The boy's father, grandfather, and an uncle suffered from paralysis agitans. Following an attack of influenza with fever, the boy showed a weakness of the left arm and leg. On examination the following symptoms were found: Patellar and Achilles reflexes greatly increased; Babinsky and Oppenheim signs positive on both sides; marked paresis of the left arm and leg, and slight paresis of the right leg. After treatment for two and one-half months the disease had advanced rapidly. The left arm was completely spastic and paralyzed, and the muscles atrophied. The muscles of the left leg showed characteristic rigidity. Paresis was marked in the right leg and beginning

paresis was present in the right arm. There was stammering speech, frequent aphonia and constant swallowing; widening of the palpebral fissure and paralysis of the abducens, the latter of rare occurrence in this disease. The symptoms increased in severity until the child's death two months later. Sensibility remained intact throughout the course of the disease. On the basis of a congenital weakness of his motor system, the child developed, through a febrile infectious disease, a typical symptom complex of lateral sclerosis. It is possible that the febrile attack was not influenzal, but the febrile reaction of the onset of lateral sclerosis. The unusually rapid course of the disease is remarkable. According to Oppenheim the usual duration is from two to four years; in this case it was only five months.

OBSTETRICS

UNDER THE CHARGE OF

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The Treatment of Eclampsia.—LICHTENSTEIN reports from Zweifel's clinic in Leipsic the results in the treatment of 400 cases of eclampsia (*Arch. f. Gynäk.*, 1911, Band xcv, Heft 1). He finds that in all eclamptics convulsions cease in but one-third of the cases after pregnancy has been terminated. The common belief that eclampsia occurring in the puerperal period has a low mortality rate was shown to be incorrect. The mortality of the induction of labor is not better than that following the rapid emptying of the uterus, and the mortality of both procedures does not differ especially from the general mortality of a large series of cases. The most modern statistics are not favorable to the emptying of the uterus. The difference in the mortality between eclampsia before and after labor seems to depend upon the relative loss of blood, and this is from 100 to 150 c.c. of blood more than the average loss in labor. In 40 per cent. of eclamptics operated upon, the average blood loss of eclampsia, reckoned at 500 c.c., is exceeded during operation; while in those who are delivered spontaneously there is no increase in the blood loss; 52 per cent. of eclamptic patients operated upon have a greater blood loss than that occurring in normal labor; while but 4 per cent. of eclamptics delivered spontaneously exceed the average blood loss of parturition. Those patients in whom convulsions cease after delivery lose one-half more blood than those in whom the convulsions do not cease, and four times as much blood as those in whom the convulsions first develop during the puerperal period. The significance of blood loss is seen most strikingly in its tendency to produce collapse. If the loss of blood in eclampsia is to be beneficial, it is better that blood be taken before the uterus is emptied, instead of encouraging bleeding during the rapid termination of pregnancy. That the interruption of pregnancy in eclamptic

patients is not imperative is proved by those cases in which the eclampsia ceases and the pregnancy continues to its normal termination, often with the birth of a living child. When one attempts to reason concerning the placental theory of eclampsia, by comparing the results of rapid delivery and induced labor in eclampsia with former statistics, the placental theory receives from this source no support. Cases of intercurrent eclampsia do not support the theory that eclampsia is produced by the product of conception. It is further observed that eclampsia often first develops during or after the birth of a macerated fetus, which must have been dead for some time. In the psychoses which follow eclampsia, it is found that these patients have two or three times as many convulsions as the general average—eight for each patient. In 50 cases which came to autopsy, dilatation of the ureters and pelvis of the kidney was found in 30 per cent.; while in 27 patients operated upon before death, it was found present in $33\frac{1}{2}$ per cent.

The Vaginal Extirpation of the Pregnant Uterus in Phthisical Patients.—HEIL (*Zentralbl. f. Gynäk.*, No. 44, 1911) has operated upon 7 cases. One of these died of phthisis six months after the operation; 3 survived from one year to one year and one-half, and are still in good condition; in 2 the pulmonary condition is markedly improved; while in the last case operated upon the tuberculosis seems to have made progress. In selecting patients for operation he would take those who have already given birth to children now several years old and in good condition. The tuberculous process in the lungs must be clearly defined and increasing. The lung tissue must not be hopelessly diseased, for should this be the case substantial improvement cannot be expected. He prefers vaginal total extirpation of the uterus to operations upon the tubes, because the latter are not absolutely certain in their results. In multigravidæ two or three months advanced the operation is especially successful. In later pregnancy the anesthesia and blood loss are unfavorable. In recommending this method of treatment, Heil accepts the reasoning of Martin, who more than a year ago urged the adoption of this procedure.

Rupture of the Uterine Scar after Classic Cesarean Section.—VOGT (*Arch. f. Gynäk.*, 1911, Band xcv, Heft 1) contributes an interesting paper on this subject. His observations were made in Leopold's clinic in Dresden, and he reviews to some extent the literature on the subject. He distinguishes between the time before antisepsis and the period subsequent to this when antiseptic and aseptic precautions have been observed. In the first period up to 1886, Krukenberg had collected 18 cases of rupture of the scar after Cesarean section. At this time the uterus was not sutured after operation, and Krukenberg believed that the scar ruptured in 50 per cent. of these patients who again became pregnant. Winckel observed 4 cases of rupture in subsequent pregnancy in labor. Afterward Saenger, in 1882, urged the exact closure of the uterus by suture. In 1895 he reported that in 500 cases where the uterus had been exactly closed, rupture in the scar had been observed. After this the operation was taken up by many operators, some of whom were unskilled surgeons, and in 1905 Werth had collected 12 cases of rupture. In 1908 Hartmann collected 18

cases, and since then others have in all found 22 cases. Among the French, Couvelaire in twenty years had collected 8 cases. In 183 operations von Leuwen found four ruptures. Vasseur estimated that rupture occurred in 2 per cent. of cases. Excessive amniotic liquid and twin pregnancy predispose to rupture. The attachment of the placenta beneath the uterine scar is also favorable to this accident. The site of the uterine incision seems to have no influence upon rupture, for it occurs in both the longitudinal and transverse incision. So far as suture material is concerned, rupture has been observed in cases where silk was used, silk and catgut, and catgut alone. It is observed that cases which heal without infection and by primary union are much less apt to rupture than those in which infection develops and union is secondary. There is very much more in the method of applying sutures than in the choice of suture material. An experienced and skilful operator who closes the uterus accurately and thoroughly will have a very small percentage of ruptures in the scar. It is, however, true that the possibility of rupture in subsequent pregnancy can never be entirely eliminated. This is true if gonorrheal infection has been present at the time of the original operation, or subsequently. In clinics having the largest number of operations, the smallest percentage of ruptures has been reported. Olshausen, in 120 cases, observed rupture in the scar but once; Braun, in 77, in none; Everke, in 64, in one; Chrobak, in 64, had none; Schauta, in 177, had none; Küstner, in 100, had none; and Leopold, in 232 cases, had no case of rupture in the scar. As regards cases of repeated section, Olshausen, in 29 cases, had operated upon 2 patients twice, and upon 3 patients three times. In the Leipsic clinic, in 54 cases, there were 11 done a second time and 4 done three times. Braun, in 74 cases, did the operation twice on 5 patients, and three times on one patient. Küstner, in 104 cases, operated twice on 10 and three times on one. Leopold, in 229 cases, had 15.5 per cent. of repeated section. Birbaum operated four times upon a patient successfully, but after the fifth operation the patient died of pulmonary embolus. Braun and Vogt have reported cases of induced labor after Cesarean section in which the uterine scar remained sound. Spontaneous labor after Cesarean section is comparatively rare, Braun reporting but 3 cases, and Abel, from the Leipzig clinic, but 2 cases. In an ape that had been subjected to section a spontaneous labor with living young afterward occurred. In cases where the subsequent labor is terminated by the use of forceps, or by version, the scar is naturally put to the severest test. Krobak did version in 2 cases, in 1 of which symphysiotomy preceded version. Abel had 3 induced labors after section, and in 2 cases embryotomy was performed. To illustrate what such a patient can endure without injury, Vogt reports the case of a woman having a flat rachitic pelvis with a true conjugate of $6\frac{3}{4}$ to 7 cm. She was delivered three times by craniotomy, once by version, in the fifth and sixth pregnancies by Cesarean section. In the seventh pregnancy the patient had twins, one of which was born spontaneously, the other developing the transverse position. In the eighth pregnancy version and perforation of the after-coming head were performed. In the ninth pregnancy the patient declined any operation, and after fourteen hours of labor in Walcher's position the head was brought by pressure through the pelvic brim, and a child 52 cm. long and weighing

3000 grams was delivered. The cranium showed the results of pressure, but the child recovered and subsequently became vigorous. This delivery was preceded by version, and an excellent opportunity was given to test the firmness of the scar. The mother made an uninterrupted recovery. In Lihotzky's case, five years after section the patient had induced labor. Rupture did not occur in the old scar, but in the uterine muscles some distance from the scar. Krukenberg reports 3 similar cases. Füh performed section upon a patient who had an incarcerated dermoid cyst in the pelvis which prevented delivery. In the second labor, as the pelvis and the size of the child were normal, no operative interference was practised, but the uterus ruptured, not in the scar but near the place of entrance of one of the Fallopian tubes. A similar case occurred in the Dresden clinic in a patient who had been delivered by section two years previously for eclampsia. In a second pregnancy induced labor was undertaken outside the clinic, and the patient was brought to the hospital with symptoms of peritonitis. On performing section the child and placenta were found in the abdominal cavity, and the uterus ruptured through the right cornu, but not in the old scar. A Porro operation was performed from which the patient made a good recovery. The mortality of this accident is estimated by Scipades as about 45 per cent. In the collection of 22 patients, 3 died—a mortality of 13 per cent.; in 8 the wound in the uterus was again united; in 13 some method of amputation was practised. The prognosis for the child is naturally bad; 31 per cent. are saved by prompt operation. It is important in these cases to know how great has been the first blood loss, and whether, when the patient is seen, the bleeding has ceased or is going on. The second point depends upon whether the ovum has been totally expelled or partially retained. If the placenta has been delivered, the empty uterus contracts and bleeding from the placental site ceases. The point of rupture usually bleeds but little. In some cases the primary blood loss is sufficiently great to be fatal. Occasionally patients are able to walk or to be carried for some distance after the accident. In one case the patient did not collapse until the bursted uterus contracted upon a loop of intestine which had prolapsed into its cavity. Microscopic studies of these cases show that where union is successful muscular tissue develops so perfectly that no trace of the original scar can be found. Where muscular tissue is lacking and the connective tissue replaces it, the danger of rupture is greatest. It is the opinion of experienced operators that at the present day so perfect is the technique of the operation that the danger of subsequent rupture is very slight. In 162 cases of cervical section Holzapfel had no case of rupture of the scar. Traugott found the cervical scar greatly thinned and dilated in a case subjected to a second operation. Sellheim has also seen a similar case. A study of this subject leads one to conclude that in order to prevent rupture of the scar the uterus must be accurately and thoroughly closed and heal without infection. A patient who has had a section, and with whom the possibility of conception remains, should pregnancy again occur, should be under the observation of a physician, and convenient to a clinic. In the event of rupture, operation should be done as quickly as possible, and the operator must decide whether he will endeavor to save the uterus, or remove it. A classic Cesarean section is not only a life-

saving operation for the child, but in the hands of skilled operators is especially such for the mother. Rupture of the scar, after an operation properly performed, is exceedingly rare, and with good surgical attention has a very favorable prognosis.

Hemolysis by Streptococci in the Vaginal Secretion of Pregnant and Parturient Patients.—A contribution to this complicated and controversial subject is made by LAMERS (*Arch. f. Gynäk.*, 1911, Band xcv, Heft 1). His experiments lead him to conclude, with Frommes, that the germs found in a particular patient are harmless to that patient, even though they may be in a condition favorable for the development of hemolysis. Those germs which are transferred from without to a patient are the real producers of severe infection. The mere occurrence of hemolysis does not make the difference between these germs, but is a question as to the energetic growth of the bacteria. It is the relation of the germs to the patient which is important. We have as yet no method of determining accurately whether a given germ is potent or inert to a given patient. Lamers concludes that hemolytic streptococci are found in the genital tract, and in the secretions of pregnant patients, not as a rule, but as an exception to the average. The presence of hemolytic streptococci in the lochial secretion cannot be explained as an increase of germs already present during pregnancy, nor is it probable that these germs were introduced by examinations made during labor; it is also not probable that these germs arise from the ascent of bacteria during confinement or the puerperal period. In pregnant parturient and puerperal women, one often observes colonies of greenish streptococci weakly hemolytic, which must be considered as intermediate forms between those which are not hemolytic and those which are. It seems probable that the hemolytic can develop from the non-hemolytic. Those hemolytic streptococci which develop without disturbance to the patient, and without fever, seem to come from the non-hemolytic germs. On the contrary, those which do produce fever and other symptoms arise from germs introduced from without. Hemolysis produced by streptococci does not depend so much upon the individual germ as upon the surroundings favorable for its development.

GYNECOLOGY

UNDER THE CHARGE OF

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Relation of Ovulation to Menstruation.—FRAENKEL (*Zentralbl. f. Gyn.*, 1911, xxxv, 1591) has found by observations made during abdominal operations for extragenital conditions that a fresh corpus luteum is never found in the ovaries when the operation is done during the period of menstruation, therefore ovulation and menstruation do not

necessarily occur together. In 43 cases where a fresh corpus luteum was present the time which had elapsed since the beginning of the last preceding menstrual period varied from eleven to twenty-six days, but the average of most cases was eighteen to nineteen days. Allowing four days for formation of the ripe corpus luteum, this may be considered to begin to functionate about ten days before the following menstrual period. Fraenkel considers the corpus luteum the causative factor in bringing about the premenstrual changes in the uterine mucosa and in causing menstruation, and points out that its beginning to functionate about ten days before the next succeeding menstruation corresponds well with the Hitchman and Adler doctrine of the premenstrual alterations of the endometrium. The formation of the corpus luteum occurs, therefore, in the *intermenstruum*, in the second half of the interval between two periods, so that while ovulation and menstruation do not occur together, they do stand in direct time relation to each other. Fraenkel makes an appeal to all surgeons who have the opportunity to make observations along this line to do so and record their results, as only from a large amount of material can trustworthy conclusions be obtained.

Ascending Kidney Infection.—An attempt has been made by SUGIMURA (*Virchow's Arch.*, 1911, ceevi, 20) to demonstrate the method by which acute non-specific bladder inflammations reach the kidney. For this purpose he examined 21 cases, removing at autopsy the kidneys, ureters, and bladder together, and taking in each case microscopic sections from the pelvis of the kidneys, various portions of the ureters, and the bladder wall. In 4 of these cases the organs were apparently healthy, in 12 an acute bladder inflammation was present, but the pelvis of the kidneys were macroscopically free, in 5 a severe inflammation of the upper urinary tract was present, associated with a more or less chronic cystitis. In the cases of apparently normal organs no inflammation of importance was found in the ureters. In those of acute cystitis the muscularis, adventitia and submucosa of the ureters almost without exception showed, at least in the lower portion, many small foci of inflammatory infiltration which were in direct connection with those of the bladder wall. The mucosa itself was found, on the other hand, to be practically free from all signs of inflammation, such as might have been expected to be present if the infection had travelled through the lumen of the ureter. Sugimura believes, therefore, that an acute infection of the bladder ascends chiefly through the lymph vessels of the ureters, since a direct connection between the lymph vessels of the bladder wall and of the lower portion of the ureter on the one hand, and between the kidney and the ureter on the other, has been demonstrated, so that the kidney and bladder are really in communication with each other through the lymphatic vessels of the ureters. He believes further that the inflammation ascends more or less in direct proportion to the anatomical changes in the bladder wall, to the duration of the disease, and to the virulence of the causative agent. In the cases of chronic, non-specific descending inflammation with or without stagnation of urine, the important part played by the lymph vessels could also be demonstrated, although here the mucosa appeared to be somewhat more involved than in the cases of ascending infection.

Trypsin in the Uterus.—Continuing the work of Halban and Frankl, which appeared somewhat over a year ago, with regard to the presence of a proteolytic ferment in the endometrium of the menstruating uterus, FRANKL and ASCHNER (*Gyn. Rundschau*, 1911, v, 647) have attempted, by somewhat different methods to those previously employed, to determine the relative quantities of such ferments in the endometrium at the different stages of the menstrual cycle. This was done in the following manner. By means of a sharp eurette the endometrium was scraped out of freshly extirpated uteri, mixed with quartz sand, and thinned with ten times the quantity of distilled water. This was rubbed until fine (about five minutes), and was allowed to stand for twenty-four hours in the ice box; it was then filtered, and to 2 c.c. of the filtrate were added 2 c.c. of a 50 per cent. weakly alkaline solution of peptone ("Seidenpepton"). The mixture was set away in calibrated centrifuge tubes in an incubator at 37° C. for twenty-four hours, whereupon there occurred a separation of yellowish-white crystals, which could be identified by various tests as tyrosin. By means of control experiments Frankl and Aschner have found that, within certain limits, a certain quantity of trypsin throws down from a given quantity of peptone a definite amount of tyrosin within a given time, so that a fairly satisfactory quantitative determination of the amount of trypsin present is possible by this method. In interpreting the findings, however, the chief weight must be laid on the *relative* quantities rather than on actual amounts. Forty cases, in each of which the exact clinical history was known, were examined by this method. It was found that in the interval the trypsin content of the uterus is very variable, the formation of the ferment beginning in one case earlier, in another later; it always increases toward the end of the interval, however, and in the pre-menstrual stage is always very considerable. In the postmenstrual stage trypsin is almost lacking under physiological conditions; under pathological conditions, however, such as glandular hyperplasia, it can be present in quite considerable quantities. Inflammatory processes accompanied by suppuration often cause a marked increase in the ferment content of the endometrium; chronic non-purulent processes do not have much effect on it. Frankl and Aschner believe that the phenomenon of menstruation is due to the pouring out in the pre-menstrual stage of this ferment, which is then *activated* by the physiological hyperemia present, as has been demonstrated by the experiments of Rosenbach. The ferment thus activated causes a swelling of the stroma-cells, a digestion of the walls of the superficial capillaries of the endometrium, and is also responsible for the non-coagulability of the menstrual blood.

Function of Ovary in Menstruation.—HALBAN (*Zentralbl. f. Gyn.*, 1911, xxxv, 1585) considers that rut in animals and menstruation in women are very closely analogous. It can be shown that rut occurs in frogs and other animals even after castration, but it does not reach so full a degree of development as in normal animals. The same is true of menstruation—in a certain number of cases cyclic molimina and even bleeding occur for some time after the removal of both ovaries. Halban believes, therefore, that neither the sexual gland itself nor any secretion from it is the fundamental causative factor in

the production of menstruation or of rut, but that these are due to some totally unknown agency which profoundly affects the whole body; the effect of this agency can only reach its full development, however, when the sexual gland is present. This therefore exercises a "protective," but not a "formative" role on the phenomena of menstruation.

Function of the Ovary.—ADLER (*Arch. f. Gyn.*, 1911, xcv, 350) has carried out a series of most elaborate experiments in the attempt to throw additional light upon this question. He has found that in most cases of amenorrhea, in women past the menopause, and in patients upon whom double oöphorectomy has been performed, the coagulation-time of the blood is distinctly longer than in normal individuals. He has also found that in the same subject the coagulation-time is increased after double oöphorectomy as compared with what it was before the operation, and believes that it is dependent upon a condition of hypofunction of the ovaries. Since it has been shown that the coagulability of the blood is dependent, among other things, upon the presence of lime, and since it is well known that there is a close relationship between the genital glands and lime metabolism, as is shown by the improvement that occurs in cases of osteomalacia after castration, it is natural to think that the lengthening of the coagulation time caused by reduction in the ovarian activity may be due to changes in the calcium metabolism in the body. Adler has found by a series of careful analytical tests that the lime content of the blood is reduced after castration, and also after x-ray treatment of the ovaries, and believes therefore that an intimate relationship exists between ovarian function, the amount of lime in the blood, and the coagulability of the blood. Adler has not been able to produce any apparent effect on the blood pressure by injecting extract of corpus luteum or of ovarian tissue, but did get a rise after the use of pressed ovarian juice. In a young girl whose menstruation had always been absolutely regular he was able to cause the periods to occur 4 days ahead of time, to be much more profuse than normal, and to last one day longer, by giving ovarinin for three weeks preceding the period. He has been able to produce with great regularity in animals the anatomical conditions of the uterus characteristic of rut—hyperemia, gland activity, etc.—by subcutaneous injections of various ovarian preparations, and by similar treatment of human patients has been able in many instances to cause a reduction or disappearance of the subjective symptoms of the menopause. In some cases of amenorrhea ovarinin treatment has been followed by the appearance of menstruation, in these cases microscopic examination of the endometrium showing typical menstrual changes, so that the bleeding cannot be considered merely the result of hyperemia. In conclusion he says that his investigations have shown the general type of individual to be dependent, not upon one, but upon a harmonious coördination of all the organs of internal secretion. He thinks that perhaps much which appears to be due to alterations in ovarian function is really the expression of disturbances in other organs; the ovary must be considered as the centre for the genital sphere, as a centre, however, which not only sends out independent impulses, but which also transmits impulses that it receives from the intimate and complicated system of ductless glands.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF
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Reflex Affections of the Tonsil.—FAULKNER, in a paper on "Reflex Affections of the Tonsil" (*New York Med. Jour.*, August 5, 1911), deprecates the too great prevalence of tonsillectomy, and suggests that the tonsils are often sacrificed unnecessarily.

Non-communication of Frontal Sinus and Nose.—FULLERTON reports (*Jour. of Lar., Rhinol., and Otol.*, August, 1911) a case in which, while performing a Killian operation on the right frontal sinus, he entered a smaller left sinus containing pus and granulation tissue, but apparently without any detectable communication with the nasal fossa.

Killian's Operation in the Sinuses.—In discussing the subject of fatalities after this operation, SYME (*Jour. of Lar., Rhinol., and Otol.*, August, 1911) expressed the opinion that the danger in Killian's operation was probably too thorough curettage of the ethmoidal regions, and therefore he considered it better to attack the ethmoid intranasally and cautiously, and to adopt Killian's procedure for the frontal sinus alone.

Meningeal Complications Resulting from Diseases of the Accessory Nasal Sinuses.—STUCKY reports (*Kentucky Med. Jour.*, June 1, 1911) 16 cases of meningeal and cerebral complications involving the silent area of the brain (anterior frontal cerebral lobes) as result of ethmoidal, sphenoidal, and frontal sinus disease. Sixteen were reported, including 6 recoveries and 10 deaths, and the result of 8 autopsies are given. Among the complications it is noted that the infection originates primarily in the ethmoid cells—or their offshoot, the middle turbinated bone—the frontal and sphenoidal sinuses becoming involved secondarily, either through extension by continuity of tissue, or by blocking of their natural openings for drainage and ventilation long enough for their retained secretions to become purulent.

Removal of a Bullet Embedded in the Cribriform Plate of the Ethmoid.—DOS SANTOS reports (*Revue Hebdomadaire de Lar., d'Otol., et de Rhinol.*, June 17, 1911) a case of attempted suicide in whom, by radioscopy, a bullet was found to have become embedded in the cribriform plate of the ethmoid, whence it was removed by external access.

Cerebral Abscesses Complicating Suppuration of the Nasal Sinuses.—ONODI (*Jour. of Lar., Rhinol., and Otol.*, August, 1911) alludes to the statistics he has collected of 106 cases, 82 of which were secondary to frontal sinusitis, 11 to ethmoidal disease, 4 to antrum suppuration, and 1 was secondary to sphenoidal disease. Twenty-five cases of cured extradural abscess following frontal sinus suppuration were on record,

and among these there was one case in which exploratory puncture of the brain had been performed, with a negative result. In 7 of these cases the posterior wall of the frontal sinus had been perforated, and in 11 cases it was found to be diseased. In 20 of the cases of brain abscess the posterior sinus wall had been perforated, and in 57 of the cases it was diseased. In the majority of the cases the brain abscess was situated in the frontal lobe; three times it was found in the temporal lobe, once in the pedunculus cerebri, and once in the cerebellum. Of these 106 cases of brain abscess, 12 recovered as a result of operation and 29 died in spite of operation. Exposure of the cranial cavity through the ethmoidal cells in life had not yet been carried out.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Organic Matter in the Expired Breath.—WEICHARDT, of Erlangen (*Arch. f. Hyg.*, Band lxxiv, Heft 5, p. 185), calls attention to the fact that the numerous researches of Flügge and his school have shown that the very smallest bodies, such as the tubercle bacilli, can be thrown off in the expired breath during speech, coughing, or forced expiration. He believes it is self-evident that other movable particles in the respiratory tract, such as protein substances and other split products, may also be brought up and be discharged during expiration. It is obvious that fermentative processes go on in the excretory products of the respiratory tract, especially in older persons. The bronchial mucus of corpses is especially rich in toxic substances. This may be shown by injection into laboratory animals, such injections causing a sudden fall of temperature, slowing of respiration, and finally death. Fluids condensed from the expired air and then concentrated, when injected into mice, produce like results according to Weichardt. The Japanese investigator, INABA (*Zeitsch. f. Hyg. u. Infektionskrankheiten*, Band lxxviii, S. 1) believes these results to be due to the anisotonic nature of the fluids injected rather than to toxins or protein poisons. Weichardt collected substances from the breath of a fatigued man, aged over sixty years. In this experiment he collected substances from the residual air, so far as possible, by passing the expired breath for two or three hours into 10 c.c. of distilled water to which was added 0.3 c.c. NHCl. The whole was quickly concentrated in vacuo to about 2 c.c., then neutralized with NaOH and divided into two parts; 1 c.c. of this solution, which is isotonic, was injected into a mouse, resulting in a sudden fall in temperature and slowing of respirations, characteristic signs of kenotoxin poisoning. The other

cubic centimeter was evaporated into dryness, and the residue taken up in 1 c.c. of distilled water and injected into a mouse without toxic effect. This is given in answer to Inaba's criticism that the results are due to anisotonicity. Weichardt also claims to have detected the presence of split proteins by experiments in vitro. The vapors from the expired breath of a fatigued old man, aged sixty-three years, were filtered through cotton and passed through 10 c.c. distilled water and then concentrated in vacuo to 3 c.c. Likewise 10 c.c. of distilled water was concentrated to 3 c.c. The two different solutions were then carried to dryness in a tared dish. The dish containing the distilled water left no visible or weighable residue. The solution containing the products of the expired breath left a residue weighing 9 mg. This residue turned brown when heated on the platinum foil and gave off odoriferous fumes. Weichardt also notes that a characteristic odor is produced when the solution of respiratory products acidified with hydrochloric acid is neutralized with sodium hydroxide. Weichardt presents further evidence of the presence of organic matter in the expired breath by means of its inhibitory power on the action of oxidizing ferments in blood. The oxidation of guaiac by blood is inhibited by the substances found in the expired breath just as diphtheric toxin, tetanus toxin, and kenotoxin prevent the same reaction. The experiment designed to demonstrate this fact consisted in constructing a series of tubes containing 1 c.c. of the fluid containing the products from the expired air. To each tube was added a convenient amount of very dilute solution of fresh blood and 0.1 c.c. guaiac indicator. Weichardt claims that the presence of this organic compound may also be found in the air of a closed sleeping room in which there are several persons. He exposed 0.25 gram of finely powdered calcium chloride in a platinum dish covered with filter paper to keep out gross particles. The next morning the calcium chloride was dissolved and the protein-split products believed to be kenotoxic in character may be demonstrated in the solution by means of the inhibition of the guaiac or epiphanin reaction. The epiphanin reaction depends upon variation in diffusion rates in the presence of antigen and antibody combinations. Barium hydrate and sulphuric acid are used with phenolphthalein as the indicator. The method is described in the *Deutsch. med. Woch.*, 1911, No. 4. Weichardt concludes that substances which are able to inhibit such an important function as the oxidase reaction of red blood coloring matter should not be longer overlooked. ROSENAU and AMOSS (*Journal of Medical Research*, September, 1911, vol. xxv, No. 1, pp. 35 to 84) have, through the reaction of anaphylaxis, recently come to the conclusion that the expired breath contains organic matter.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

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THE
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APRIL, 1912

ORIGINAL ARTICLES

JEJUNOSTOMY.

BY WILLIAM J. MAYO, M.D.,

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JEJUNOSTOMY is an operation of considerable usefulness; it gives rest to the stomach and maintains good nutrition. The operation is an active competitor of gastrostomy in cases of esophageal and cardiac obstruction, and in extensive ulcers which cannot be excised and gastrojejunostomy is not feasible, it is a most valuable procedure. In malignant diseases of the stomach of the ulcerous type it offers a means of palliation.

The technique of jejunostomy is simple and easily carried out. The abdomen is opened by an epigastric incision either in the midline or to the left in the rectus muscle. The jejunum is picked up and, selecting a point from twelve to sixteen inches from its origin, a loop is drawn out of the abdomen, nicked on the convex surface (Fig. 1) and a No. 9 (English scale) rubber catheter pushed through the opening down stream until it extends about three inches inside the lumen of the jejunum (Fig. 2). This point is fixed in position by a single chromic catgut suture, the catheter is then infolded by the jejunal wall for an inch or an inch and a half by mattress sutures of linen after the plan of Witzel. The intestine is anchored to the peritoneum by two or three linen sutures in the lower angle of the incision which is closed down to the tube in the usual manner (Fig. 3) or the end of the catheter can be brought out of a small stab wound at one side of the incision, the intestine being fixed to the peritoneum on the inside by several linen sutures.

Liquid feeding may be commenced at any time and carried out for an indefinite period without danger of leakage and with a certainty that the nutritive material will pass into the assimilative tract. Leakage does not follow the removal of the tube and if it should slip out accidentally it must be replaced within twelve hours or the tract may become obliterated. All kinds of fluid nourishment are borne well in these cases—preparations of milk, eggs, meat ground fine and mixed with fluid, carbohydrates in fluid form, etc.

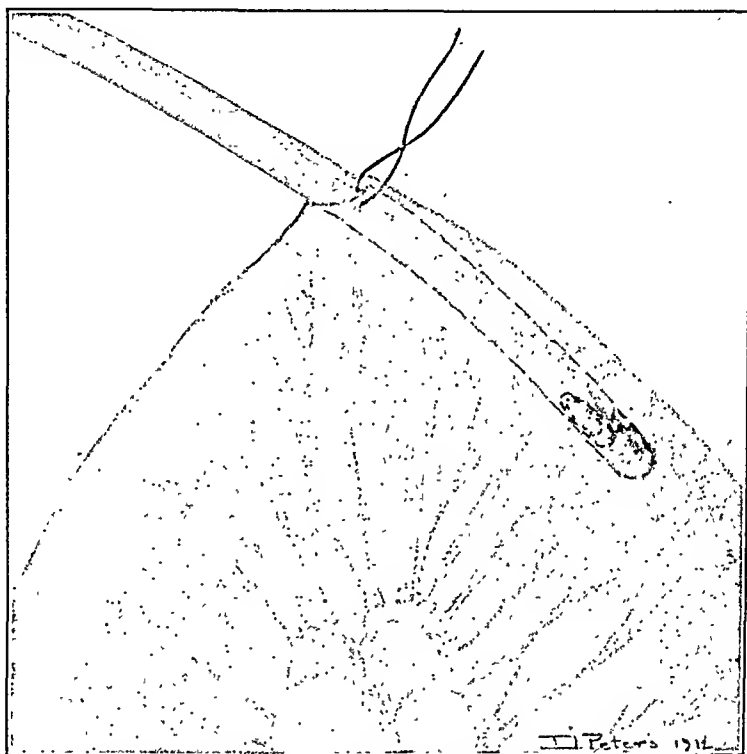


FIG. 1.—Jejunostomy: First step, showing catheter introduced into upper jejunum and fastened with a single suture.

In none of our cases have we observed subsequent ill effects from the jejunum becoming adherent to the peritoneum after the removal of the feeding tube.

In cases of esophageal and cardiac obstructions, and in diseases affecting a considerable portion of the wall of the stomach, rendering gastrostomy impossible or difficult, jejunostomy is as efficient and easier of performance than gastrostomy. It is in extensive ulceration of the stomach that jejunostomy has its greatest field of usefulness. Sometimes the stomach contains multiple ulcers, either simple or specific, in which temporary rest is indicated and gastrojejunostomy is impracticable on account of the extent

of the disease. In these cases jejunostomy affords needed rest to the stomach, a condition, it is true, which can be brought about by rectal feeding, but this procedure can in no sense be considered a building-up process; it is useful only as a temporary expedient



FIG. 2.—Jejunostomy: Second step, showing infolding of catheter.

to prolong life. On the other hand, jejunostomy improves the nutrition of the patient, a gain of from ten to thirty pounds can easily be made without resorting to forced feeding.

In this hypernutrition, with rest to the stomach lies the secret of the remarkable results following jejunostomy in some cases

of extensive gastric ulcers. One sometimes finds a large ulcer of the stomach so adherent and extensive and situated so high in the body as to render gastrojejunostomy not only hazardous, but open to the serious objection that it must be made distal to the ulcer. In such cases jejunostomy is a rational procedure, and even if the ulcer be malignant in character the method furnishes a useful means of palliation.

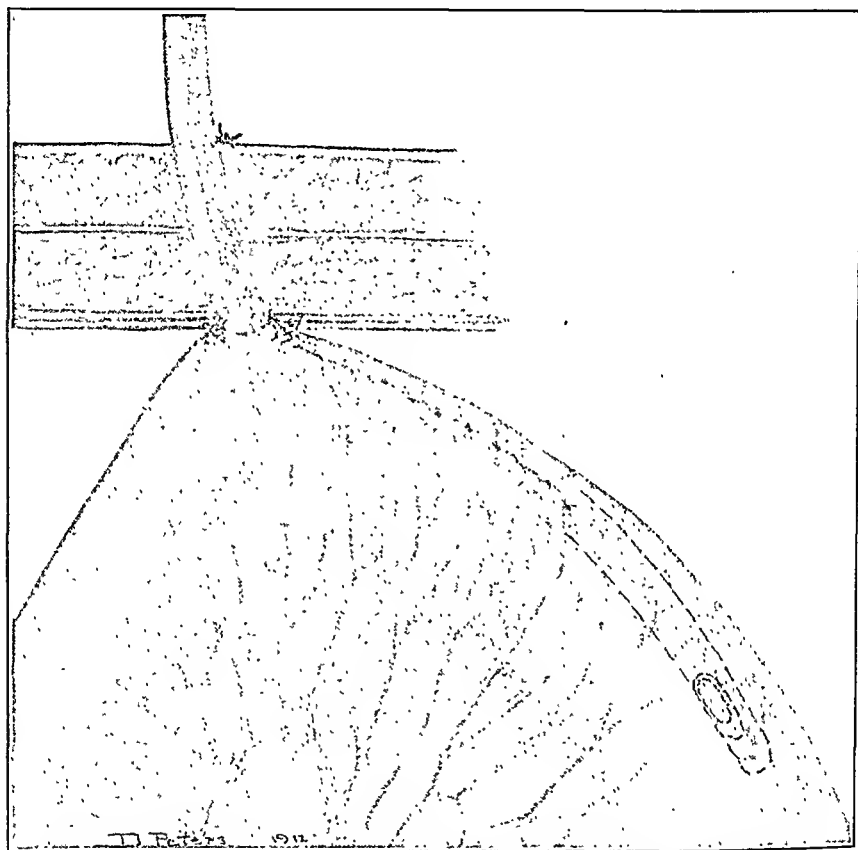


FIG. 3.—Jejunostomy: Third step, operation completed; jejunostomy fastened to abdominal wall.

Another indication for jejunostomy is in the treatment of accidental injuries to the cancerous stomach during exploration. Somewhat over a year ago while exploring a stomach which contained a large ulceration in the vicinity of the pylorus (I was trying to determine whether it was benign or malignant) I accidentally made a perforation into the foul crater of the ulcer which proved to be malignant and wholly inoperable. In attempting to repair the injury complete separation through the cancerous mass occurred. Gastrectomy was out of the question and the state of the tissue prevented the possibility of closing both ends and doing gastrojejunostomy, I therefore, reunited the cancerous tissue as best

I could with interrupted chromic catgut sutures, many of them tearing out as the tissue would not stand the strain. I then formed a sling about the line of union in the stomach with omentum, holding it in place with catgut sutures. A few rubber-tissue drains were placed about the injured stomach and jejunostomy performed. The patient was fed two months by this means. There was considerable foul discharge along the drainage tract which lasted several weeks. The catheter was removed in eight weeks, the patient gained thirty pounds in weight and lived more than a year without gastric distress and in great comfort. There was no return of obstructive symptoms in this case, although before operation the obstruction was so marked that the patient was in a chronic state of starvation and cachexia. We have observed two similar cases.

It sometimes happens, after the excision of a large ulcer of the stomach, that the organ is not in a safe condition to hold food. This is especially true of large ulcers of the posterior wall. The patients are often so debilitated that improvement in nutrition is almost a necessity in order to obtain union. Jejunostomy furnishes an easy, safe manner of giving the stomach rest during the healing process, the patient is relieved of the danger of leakage and adequate nourishment is maintained.

I am indebted to Dr. Clairmont, of Vienna, for calling my attention to the value of jejunostomy, and subsequently my interest in the operation was increased by Dr. Frank Billings, who advocated the operation on theoretic grounds, grounds which have proved correct in our clinical experience.

NOTE.—Since writing the above my attention has been called to an article in the *British Medical Journal*, January 6, 1912, by Mr. Mayo Robson in which he advocates jejunostomy in conditions of the stomach not amenable to other methods of treatment, and gives a *resumé* of his cases.

PANCREATIC LYMPHANGITIS.

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“THERE is an immense amount of sepsis in medicine.” These words of an eminent clinician convey an appreciation of the preponderating role played by infection in the production of path-

ology. The effects of infection are often obscure and far reaching, for they are indirect as well as direct, manifesting themselves at a distance as well as at the primary site, revealing their ravages at a time remote as well as immediately, and it is not too much to say that if we could attain the ambitious ideal of Pasteur of causing all the infectious diseases to disappear from the earth, that along with the so-called infectious diseases would go such a large proportion of diseased conditions, now but little considered in this connection, that our works on pathology could be condensed into the size of a primer and our occupation would be all but gone.

Still, it is our chief task to unravel the devious ways of infective disorders, since it is only by a thorough understanding of their etiology, clinical course and effects, that we may hope to palliate or cure and ultimately to prevent them. For this reason we offer this brief suggestion as to the origin of certain pancreatic swellings and inflammations.

That pancreatitis, both acute and chronic, is in practically every instance due to microörganismal invasion will hardly be denied, even though it be admitted that in certain instances systemic intoxications due to alcohol, syphilis, tuberculösis, or other unknown circulating toxins may be productive of degenerative lesions which may be classed as chronic pancreatitis. There is also reason to believe, on the basis of clinical and experimental evidence, that the retroinjection of bile into the pancreatic duct may set up acute pancreatitis of the most severe type even in the absence of micro-organisms. Hlava's experiments show that the same result may follow the injection of gastric juice into the duct, though there is no evidence that this ever occurs clinically. Even in these cases infection has been demonstrated to follow quickly in the wake of the aseptic injury, and under conditions as they are found in the body, infection must practically always precede or go hand-in-hand with the entrance into the duct of any foreign material. Giving these considerations all due prominence, it still remains an incontrovertible fact that pancreatitis is for all practical purposes a consequence of infection, our conclusion being based not only upon analogy, but upon cultural examinations in acute inflammations, upon its frequent association with frankly infective processes in neighboring viscera, and upon the microscopic evidence of infection in the gland itself.

The chief point at issue is the method by which infection gains entrance to the gland. There are the following possible portals of entry: (1) The systemic circulation, through the arteries of supply. (2) By contiguity from adjacent viscera. (3) Ascending infection of the duct from the biliary tract or duodenum. (4) Through the lymphatics.

1. There is but little evidence in favor of infection by way of the circulating blood. The frequency of bacteremia and pyemia and the rarity of involvement of the pancreas in these conditions establishes our belief in almost complete immunity of the pancreas against serious infection through the blood stream. The clinical history of cases who are the subject of pancreatitis also furnishes no warrant for a belief in this mode of origin. When it does occur it must be classed as a rare exception.

2. Instances are not rare in which the pancreas is involved in inflammation by direct extension from a neighboring organ. The most frequent example is the chronic perforating ulcer of the stomach or duodenum which eventually makes its bed in the pancreas. In such cases the pancreas protects itself by granulation tissue and cellular infiltrate, and may suffer no general injury. In other instances it may show acute or chronic lesions more or less widespread. Bartels has reported a case of acute hemorrhagic pancreatitis associated with perforated duodenal ulcer, which is doubtless of this nature. Infection of the gland by direct contiguity is, however, relatively uncommon, the mechanism of which is simple, but fails to explain the great number of cases of pancreatitis which are now being recognized.

3. The great volume of discussion concerning the origin of pancreatitis deals with the noxious influences that may be brought to bear by way of the ducts of the gland. To stenosis or occlusion of the ducts, the injection of biliary or duodenal contents, and ascending duct infection have been assigned the chief and almost the sole part in the production of acute pancreatitis and the interlobular form of the chronic disease. Experimentally acute and chronic disease have been reproduced both by infection and by injection of the ducts. Clinically our attention has been centred upon the association of the disease with disease of the bile passages, and it has been natural to suppose that in the association of terminal facilities of the common bile duct and the pancreatic duct we have a ready means and explanation of infection of the pancreas, the affections of the latter being quite commonly accepted as being secondary to disease of the biliary tract in the majority of instances.

There are certain objections to this facile explanation. First, it is observed that the pancreas is often diseased without demonstrable disease of the biliary apparatus. In the senior author's experience about one-third (36 per cent.) of all instances of chronic pancreatitis, and 25 per cent. of acute cases were not accompanied by demonstrable disease of the biliary passages. Most investigators have laid stress upon the more frequent association of pancreatitis with gallstones, giving almost no attention to the minority of cases in which not only gallstones but even other evidences of biliary tract infection were absent. Truhart alone found that a smaller percentage of patients with acute pancreatitis had gallstones

than those who died from other causes. Desjardins supporting the belief in ascending infection, attempts to explain this by assuming that the same infection gaining entrance into the ducts of the biliary or pancreatic system may cause at one time cholangitis, or at another, inflammation of the duct of Wirsung. This is merely an assumption unsupported by clinical evidence.

A strong objection to the similarity of causes of the two conditions is their lack of parallelism according to sex. Nothing is better established than the preponderance of cholelithiasis among females, the ratio roughly being about three to two. In the series of cases of pancreatitis above mentioned the ratio was reversed, and though percentages differ, the experience of operators the world over shows that males are much more prone to this disease than are females. This fact, while not in itself conclusive indicates that probably we have laid too great stress upon the similarity of origin and intimate relations of pancreatitis and biliary disease, and directs the attention to further inquiry into the method of origin of pancreatic affections. This additional factor and one which has received altogether less attention than it deserves, we believe to be:

4. Infection by way of the lymphatics. The validity of this explanation depends upon the existence of primary infectious processes so situated with reference to lymphatic vessels that the infection may more or less readily reach the pancreas through these channels.

Of the four great sources of intra-abdominal infection, the appendix, the Fallopian tubes, the gall-bladder, and the pyloric region, the latter two are situated in close proximity to the pancreas. If it be shown that there exists an inter-communication of the lymphatics of the pancreas with these two danger points, from our knowledge of the behaviour of the lymphatic channels as avenues of infection it would seem not unlikely that the pancreas would suffer secondary involvement. Not only the grosser lesions of the gall-bladder and juxtapyloric region, such as cholecystitis and gastric or duodenal ulcer should be considered in this connection, but also those more frequent minor infectious processes which pathologically are termed catarrhal and clinically usually fail of recognition, except under the name of indigestion or dyspepsia. In the gall-bladder we are accustomed now to recognize extremely mild grades of inflammation of the organ by the presence of ever so slight thickening, diminution in lustre, increased opacity, or inspissation and tarry character of its contents. The same scrutiny should be directed toward the stomach and duodenum where slight thickening, local puckering, or distortion and increased opacity may reveal the present or past existence of inflammation of the wall. As evidence of previous inflammation we have observed dimpling of the wall at times suggesting the starting point of an intussusception. Again, there have been delicate adhesions easily to be over-

looked, and even less prominent is a peculiar streaked, opaque appearance affecting a very limited portion of the wall and often running off toward adjacent peritoneal attachments. Of course, the grosser cicatrices of healed ulcers are readily apparent, but these less conspicuous appearances should be noted as indicating, in many instances at least, the previous existence of interstitial inflammatory processes. Catarrhal inflammation, fissures, and even early ulcers may exist without external evidence of their presence, and yet as a portal of bacterial entry their importance cannot be denied as is shown by the enlargement of the regional lymphatic glands. To those abreast of the revelations of surgery in the upper abdomen no argument is needed to convince of the great prevalence of infectious processes, the potential gates of entry of organisms into the lymphatic paths of this region. It remains to show the intimate relationship of these efferent lymphatics with those of the pancreas, and our clinical basis for believing that pancreatitis may originate in this way.

ANATOMICAL CONSIDERATIONS. The brilliant study by Bartel of the lymphatics of the pancreas must be consulted in order fully to appreciate their anatomy. This work was carried out both upon animals and human subjects, and from it we draw freely. The pancreas, unlike certain other organs, possesses no great hilus through which pass the afferent and efferent blood and lymph vessels. The lymphatics emerge at various points along its surface, and run to the regional glands, to neighboring trunks or plexuses. This arrangement should be especially noted, as it leads to a very important deduction.

It may be pointed out that by reason of its retroperitoneal situation it bears a close relation to the thoracic duct and to many trunks which empty into it from the visceral and parietal lymphatics of the abdomen. As regional glands of the pancreas, demonstrated by the Gerota method of injection, Bartel describes: The pancreaticosplenic and superior pancreatic, the superior gastric, hepatic, pancreaticoduodenal (anterior and posterior), mesenteric, mesocolic, inferior pancreatic, and peri-aortic (Figs. 1 and 2). Once he demonstrated a direct communication between a pancreatic lymphatic and the lumbar trunk, but regards this as a rarity. He never succeeded in showing a direct communication with the thoracic duct, though this had been previously described by Hoggan. To all the above groups of glands the pancreas sends lymphatic branches which may anastomose in the cellular retroperitoneal tissues with the lymphatics from the stomach, duodenum, spleen, liver, gall-bladder and bile ducts, colon, and even the left suprarenal. Probably still other intercommunications exist which were not demonstrated. Lymphatic borne infection from these areas, in order to reach the pancreas, must in most cases stem the efferent current from the pancreas, and force the valves. Here, as

elsewhere in the body, the lymphatics are wonderfully efficient in preventing this outcome. Were it not true, our chief organ of digestion could not escape grave damage in a large percentage of cases, and pancreatitis would become one of the "Captains of Death."

Only when the inter-communications of the pancreatic lymphatics with those of adjacent organs are most intimate, short in their course, and unprotected by intervening lymphatic nodes does peril commonly arise. This most intimate relationship Bartel has shown to exist with the lymphatics of the adjacent duodenum, and more recently Franke has demonstrated that the same is true of the lymphatics coming from the gall-bladder

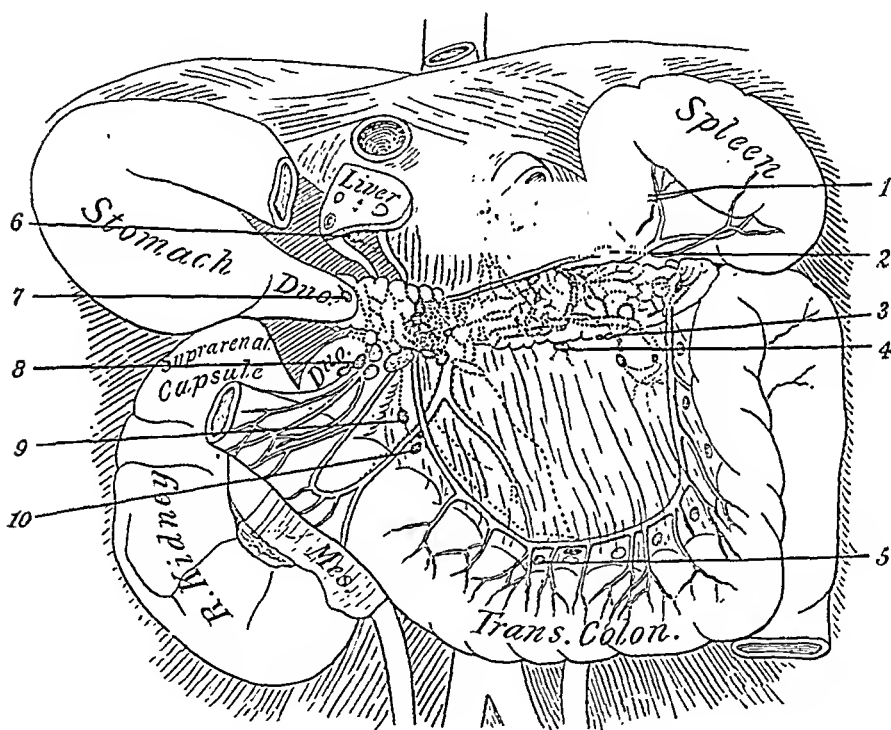


FIG. 1.—Prematurely born male child. 1, superior gastric lymph nodes; 2, superior pancreatic lymph nodes; 3 and 4, inferior pancreatic lymph nodes; 5, mesocolic lymph nodes; 6, hepatic lymph nodes; 7 and 8, pancreaticoduodenal lymph nodes; 9, mesenteric lymph nodes; 10, mesocolic lymph nodes. (After Bartel.)

How closely the finer lymphatics of the adjacent duodenum are applied to the pancreas can be appreciated by the accompanying sketch of an actual preparation (Fig. 3). The lymphatics seen upon the surface inosculate with others coming from the pancreas. In lymphatic vessels there may be a reversal of the lymph current in the effort to establish collateral circulation about points of thrombo-lymphangitis, and thus infection may be carried into the pancreas. An infection which is sufficiently severe would not even wait for a

reversed lymphatic current, but could ascend rapidly, involving not only lymphatic structures, but the surrounding tissues as well. Such a severe infection might well cause acute hemorrhagic pancreatitis by causing necrosis of the pancreatic tissue, liberating the active ferments, and eroding the bloodvessels. Bartel was acute enough to suggest on the basis of these observations, that pancreatitis might originate in this manner, but had no clinical material to support his inference, which received scanty consideration. Arnsperger has more recently, on clinical grounds, offered a similar

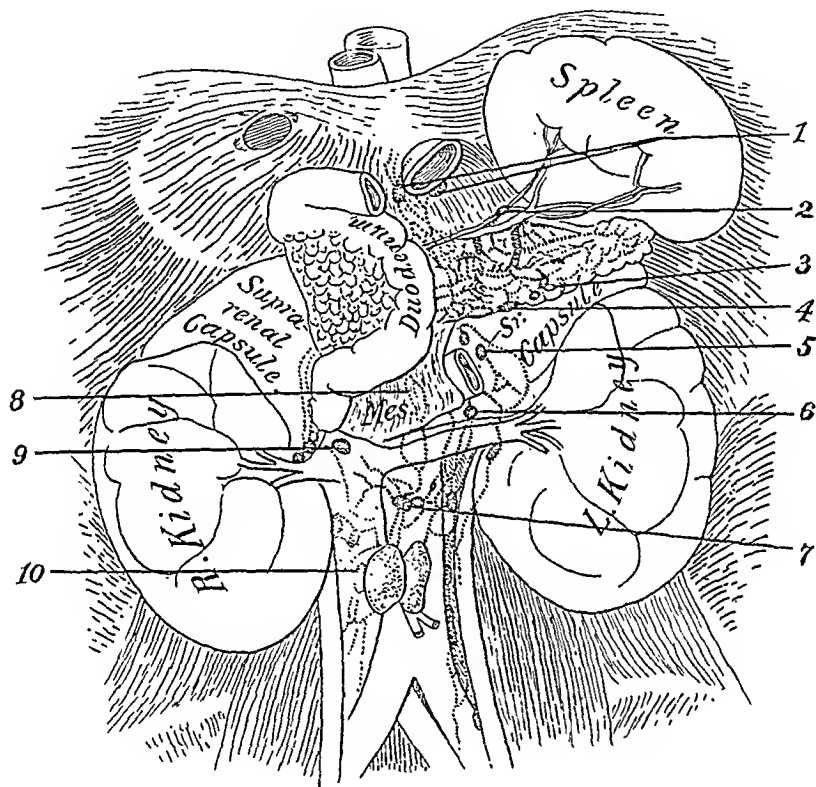


FIG. 2.—1, Superior gastric lymph nodes; 2, superior pancreatic lymph nodes; 3 and 4, inferior pancreatic lymph nodes; 5 and 6, left paraaortic lymph nodes; 7, preaortic lymph nodes; 8, from the mesenteric lymph nodes; 9 and 10, right para-aortic lymph nodes. (After Bartel.)

suggestion with reference to the association of pancreatitis and gall-bladder disease, and this view receives support from the work of Franke, who showed, also by Gerota injections, that the lymphatic vessels of the gall-bladder run to glands which lie to the left of the head of the pancreas near the choledochus, and on the right near the hepatic artery. On the way the greater part of both paths pass a gland at the neck of the gall-bladder. This gland is not, however, constant in occurrence. By injection from the gall-bladder he has filled a plexus of lymph vessels situated upon the posterior surface of the head of the pancreas. The intrinsic lymph

vessels of the pancreas run in the interlobular septa, and it is here that the effects of this type of inflammation should be most mani-

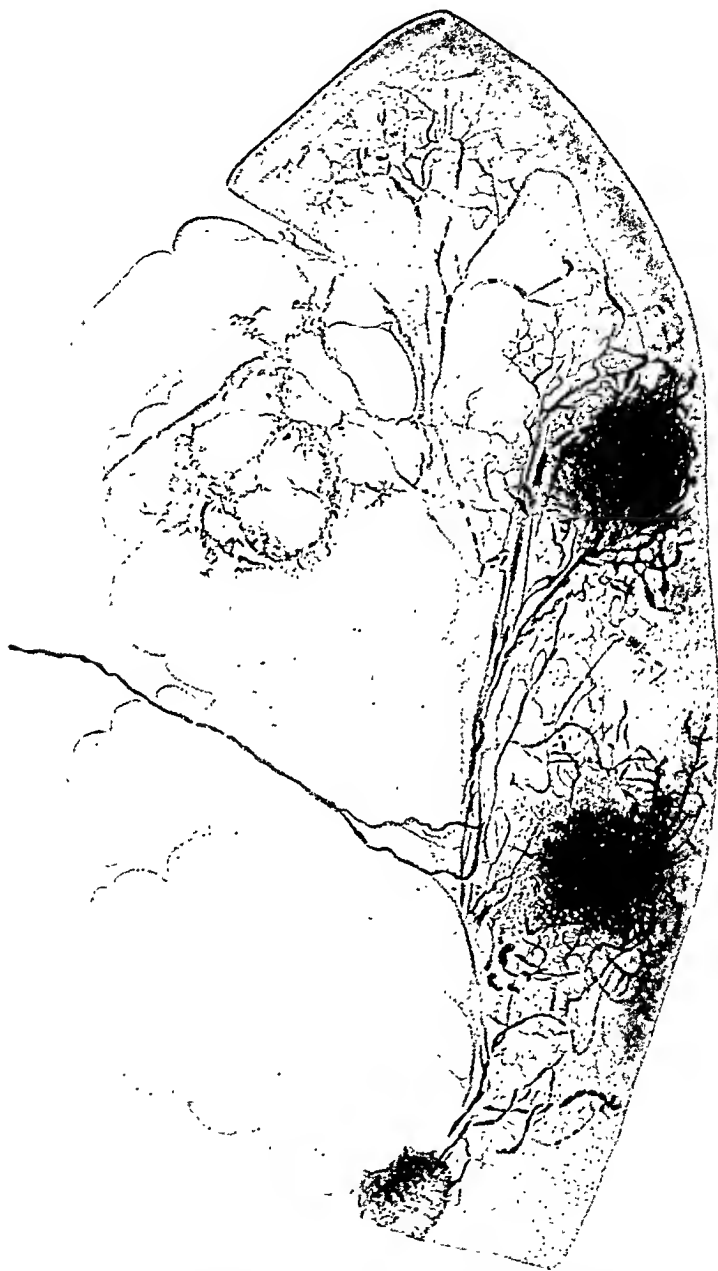


FIG. 3.—Duodenum and pancreas of newly-born dog, injected to show lymphatics. In many places an intimate connection exists between the pancreatic and duodenal lymph systems. (After Bartel.)

fest. This corresponds with the fact that the form of pancreatitis usually associated with inflammatory lesions of neighboring viscera

is the interlobular type, as contradistinguished by Opie from the interacinar sclerosis which appears to bear no such relation to local inflammation. Of itself, however, this observation does not speak for a lymphatic origin of pancreatitis since the pancreatic blood-vessels and ducts also run in the interlobular tissue, and if inflamed would produce interlobular sclerosis. A most suggestive point is the following: It is observed by all surgeons that the earlier forms of pancreatitis found at operation in connection with the gall-bladder or duct disease involve only the head or perhaps only a portion of the head. In other words, *the distribution of inflammation corresponds to the lymphatic distribution*, which, as mentioned above, is irregularly segmental. It does not correspond to the duct distribution, which ramifies by dichotomous division from the main accessory ducts. It is most difficult to understand on the theory of duct-borne infection why the gland should not more often be symmetrically involved, while if the lymphatic method of transmission be granted this phenomenon is readily explainable. Again, the swellings of the head of the pancreas which are so frequently encountered by the abdominal surgeon must be different from the varieties of chronic pancreatitis described by the pathologist. Kehr, on clinical grounds, has surmised that such a distinction exists. Chronic pancreatitis, which is characterized by interlobular or interacinar deposits of fibrous tissue, is no more curable than is chronic nephritis, or cirrhosis of the liver. On the other hand, it is characteristic of the pancreatic swellings associated with biliary disease to subside with the subsidence of the biliary infection. This swelling must, therefore, be due to edema, congestion, and absorbable infiltrates. Its subsidence on cure of the primary infection would be analogous to that which occurs in the treatment of primary foci of lymphatic infection elsewhere in the body. It may be urged by those who advocate ascending duct infection that the disappearance of pancreatic involvement occurs as the result of the cessation of reinoculation with infected bile, and it is true that of itself this observation does not speak for either mode of infection. In many of these cases, however, Nature attempts by her own method of injections to point the course of events. In this form of pancreatitis operated upon at the fortunate time it is possible to demonstrate the chain of infection; infected gall-bladder, enlargement of the cystic gland, enlargement of the glands at the head of the pancreas, and swelling of the regional lymphatic distribution of the pancreatic head. Since we have been looking for these glands it is remarkable how constantly they have been found in this condition. One which appears to be especially constant in position and enlargement is situated just to the right of the choledochus, where it passes beneath the duodenum.

We have spoken of this condition chiefly in connection with the gall-bladder because it is here most easily capable of recognition,

but it is our belief that lymphatic infection from the duodenum may play a considerable role in chronic pancreatitis. Not a few instances of the association of duodenal ulcer and pancreatitis are on record, while catarrhal duodenitis may also contribute a share. The greater frequency of duodenal disease in males would correspond with the sex incidence of pancreatitis, which is not true of biliary disease as previously mentioned.

It is possible that still other organs may at times furnish infection to the pancreas, but the biliary tract and the duodenum seem to be the most probable primary sources on anatomical, clinical, and pathological grounds.

To this early and remediable stage of pancreatic inflammation, in order to distinguish it from the advanced types commonly designated as chronic pancreatitis, it would be well to apply the term pancreatic lymphangitis. The reasons why pathologists have failed to recognize this condition are probably to be found in the fact that the postmortem lesions are slight and can easily be confused with that autodigestion of the organ which ensues at once after death, and often renders examination of its tissues unsatisfactory, and also because the clinician has not previously called attention to the necessity for search for the minor pathological changes. Moreover, the material has been small since it is essentially a process of living pathology. It is not of itself an immediately fatal disease. It may subside with the removal of the primary source of irritation as above pointed out, and when of long standing or frequent recurrence it leads to the deposit of interlobular fibrous tissue, in other words to chronic interlobular pancreatitis.

At the present time the diagnosis can be made only by the surgeon who can inspect and palpate the gland. The treatment is that of the primary focus of infection whether cholecystitis, cholelithiasis, ulcer, or duodenitis. In cholecystitis cholecystostomy is the operation of choice. A gall-bladder damaged to the extent that recovery and permanent cure are doubtful, should be removed. When the pancreas presents marked alterations cholecystoduodenostomy is superior in its results, though the mortality of operation should decide in favor of a simpler procedure unless there are clear indications for its performance.

For the evidence of this condition it is necessary to go to the operating table. We have not yet been fortunate enough to encounter a case complete in ante- and postmortem detail. The following case is cited to show the extent to which the disease may progress. The pathology is too far advanced and the etiology too obscure to prove its lymphatic origin in this instance. The glandular involvement, however, is similar in many respects to that observed by us in a considerable number of earlier cases where the considerations just mentioned lead to the belief in a lymphatic origin.

D. G., aged thirty-seven years. Admitted to the German Hospital, January 6, 1912. Died January 19, 1912.

Chief complaint, cramps in upper abdomen, radiating into flanks and to right side of back.

Family History. Mother died of tuberculosis, otherwise negative.

Personal History. Tea, coffee, and tobacco in excess; alcohol in moderation; denies venereal diseases. In March, 1910, he was admitted to the Pennsylvania Hospital suffering with pain beneath right costal margin radiating to the back. The pain was worse two or three hours after eating. Constipation was a marked symptom, and he had lost considerable weight. At operation cholecystitis was found and cholecystotomy performed. In July of the same year he was again operated upon for recurrence of symptoms and cholecystoduodenostomy performed. In June, 1910, he was again in the hospital with the same symptoms plus jaundice, chills, and fever. Cholelithiasis was diagnosed, but he was not operated upon. In November, 1910, after intermittent attacks resembling those of stone in the common duct he came to the German Hospital and was again operated upon. Chronic pancreatitis, chronic cholecystitis, and a stone in the common duct were found. The stone was forced into the duodenum. The cholecystoduodenostomy opening had become obliterated; cholecystoduodenostomy performed. Recovery was uneventful, and he was improved for a few weeks, when his trouble recurred. More recently he has been having chills, fever, and jaundice.

Physical Examination. A poorly nourished man of nervous appearance. Skin moderately jaundiced. Head and chest negative.

Abdomen: Scar of old incision through upper right rectus. In this region and in the epigastrium there is marked tenderness on pressure, but no rigidity or mass.

Urine shows a very faint trace of albumin, and a few hyaline casts, otherwise negative.

Blood: Hemoglobin, 73 per cent.; erythrocytes, 4,050,000; leukocytes, 7300; polymorphonuclear neutrophils, 73.5 per cent.; lymphocytes, 26 per cent.; eosinophiles, 0.5 per cent.; coagulation time, 8 minutes.

Stool: Dark green and practically non-odorous; fluid; neutral reaction; a trace of bile, occult blood positive to benzidine and guaiac tests. Azotorrhea and steatorrhea marked.

Cambridge reaction positive.

Operation, January 13, 1912. Dr. Deaver. Ether anesthesia. Excision of old scar in upper right rectus region; adhesions of stomach and right lobe of liver to incision; hepatic flexure of colon adherent to right lobe of liver; great omentum adherent to lesser omentum; small whitish tubercles found on small intestines; some adhesions between ascending colon and parietal peritoneum; liver covered with a few whitish nodes which are subserous;

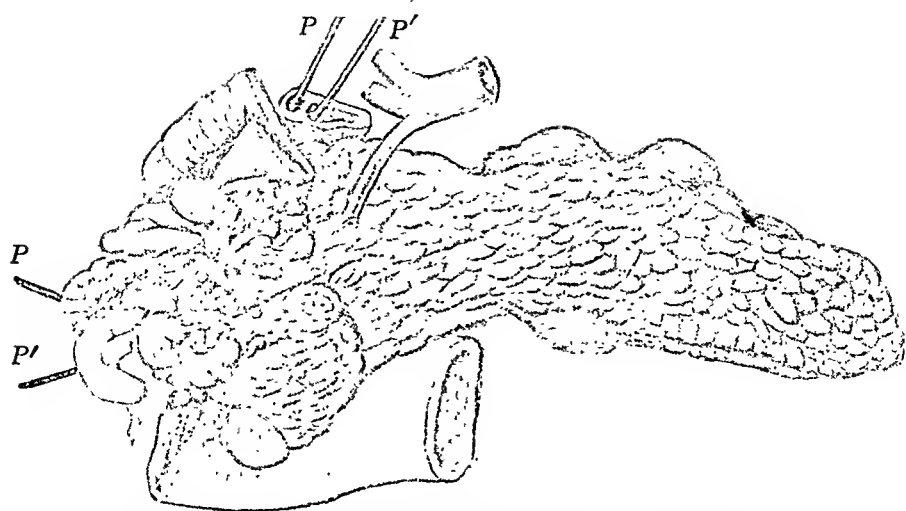


FIG. 4.—Anterior view of pancreas: *P* and *P'*, probes in choledochus and fundus of gall-bladder near gastro-enterostomy opening. Celiac axis adherent to upper margin but not in true relation. The nodules adherent to the head and upper and lower margins of the pancreas are hyperplastic lymph nodes.

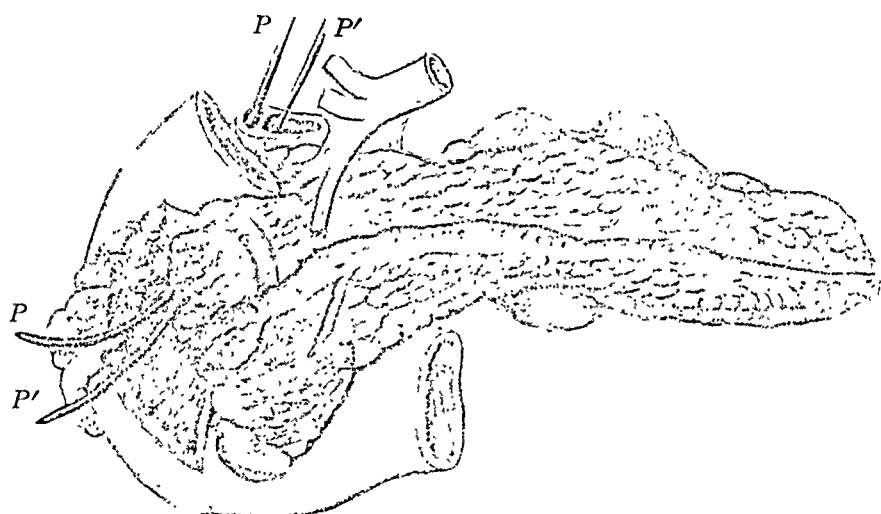


FIG. 5.—Anterior view with duct of Wirsung opened throughout its length and a window in duodenum.

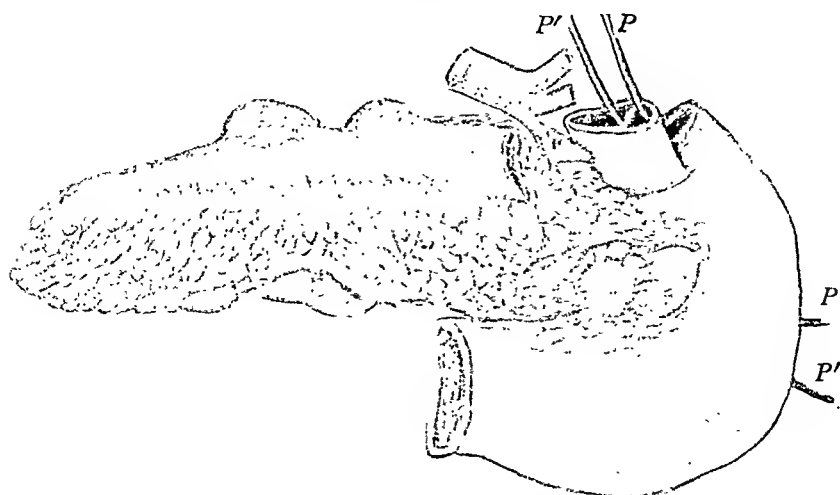


FIG. 6.—Posterior view showing enlarged posterior pancreaticoduodenal lymph nodes.

old cholecystoduodenostomy still patulous; head of pancreas enlarged and hard; felt semicystic; foramen of Winslow, though occluded, was forced open; small glandular enlargement at junction of the supra- and retroduodenal portions of the common duct; head of pancreas opened by inserting scissors and withdrawing them opened (Hilton's method). Much hemorrhage followed this; was controlled by a piece of selvage gauze and one suture of iodine gut; duodenum incised and old cholecystoduodenostomy proved patent; much bile-stained material escaped from opening; head of pancreas seemed to be obstructing the duodenum posteriorly from pressure; duodenum closed with catgut baseball suture and a Lembert of linen thread; pancreas at site of incision sutured to parietal peritoneum; one cigarette drain anterior to gastrohepatic omentum; one rubber tube at foramen of Winslow; another rubber tube anterior to this and wound closed in layers.

Following the operation there was profuse brownish drainage from the wound. The jaundice disappeared. He became more emaciated and gradually weaker and died January 19, 1912.

Autopsy through the incision permitted removal of the pancreas and adjacent tissues. The head of the organ was somewhat smaller than normal, and appeared necrotic. The selvage gauze in the pancreatic wound had ulcerated into the duodenum at the site of the ampulla of Vater. A fistula existed at the site of the exploratory incision into the duodenum. A striking feature was the occurrence of many enlarged lymph nodes along the upper margin of the pancreas. A few were present along the lower border, and in relation to the head both anteriorly and posteriorly where embraced by the duodenum.

Microscopically the tail of the pancreas was the seat of a moderate grade of interlobular sclerosis. The parenchyma was mostly degenerated, probably, chiefly due to autodigestion. The islands of Langerhans were intact. The head of the organ showed marked interlobular pancreatitis and an acute suppurative process superimposed. The parenchyma was necrotic. The islands of Langerhans persisted but were involved in the acute necrotic process. A section made through a small villous patch at the junction of the gall-bladder and duodenum (at the cholecystoduodenostomy opening) showed a marked glandular proliferation which had begun to invade the deeper tissues. The process had not extended more than 0.5 cm. from its starting point, and no metastasis could be demonstrated. The lymph nodes showed chronic and acute hyperplastic lymphadenitis.

We append this history in outline with illustrations because it shows the situation and appearance of the lymph nodes in many cases of pancreatic lymphangitis. It may well be stated in connection with this case that the lymphatic involvement was secondary to the disease of the pancreas, and indeed this is true in part at least.

We have, however, observed not a few cases in which regional enlargement of the lymph nodes was present without involvement of the pancreas so far as could be demonstrated. Again, they have been seen in conjunction with gall bladder and duodenal disease, the pancreas still being unaffected. Finally, in still other cases, this appearance has been associated with sclerosis and nodular thickening of the pancreas which we have come to believe represent the communication of infection to the pancreas by way of the related retroperitoneal lymphatics.

CHRONIC CHOLECYSTITIS.¹

BY J. RUSSELL VERBRYCKE, JR., M.D.,

WASHINGTON, D. C.

MACCARTY,² from the study of 365 cases of cholecystitis in which cholecystectomy was performed at St. Mary's Hospital, concludes that the different lesions of the gall-bladder are not definite entities, but are different degrees of the same process of reaction to irritation. He divides the cases into 8 groups: (1) Acute catarrhal; (2) chronic catarrhal; (3) papillomatous catarrhal; (4) malignant papillomatous; (5) carcinomatous catarrhal; (6) chronic cholecystitis; (7) chronic cystic; (8) purulent, necrotic. Two hundred and fifty-two, or 67 per cent., of the 365 cases were accompanied by gallstones. The chronic cases showed a large proportion of stones, while the early catarrhal conditions did not necessarily occur associated with stones.

It is to the large class of mild catarrhal cholecystitis, with or without stones, that I wish largely to confine this paper. How many people are thus affected is becoming more and more appreciated, due largely to the work of such men as Moynihan, the Mayos, Deaver, and a number of German surgeons and pathologists. By some the number of individuals having gallstones is overrated, but the great mass of physicians have been slow to grasp the real frequency of cholecystitis with or without cholelithiasis.

In Germany, as a result of the study of hospital autopsies, it has been estimated that of those dying in hospitals from all causes, 10 per cent. have gallstone and 13 per cent. cholecystitis. In England and this country it has been claimed by some that 6 per cent. have gallstone disease. Wm. J. Mayo³ is more conservative and his conclusions are more reasonable. He thinks that 3 per

¹ Read before the Georgetown Clinical Society, November 6, 1911.

² Jour. Amer. Med. Assoc., liv, 2004.

³ Ibid., lvi, 1021.

cent. is probably in excess of the truth and that one-half of 1 per cent. is a fairer estimate of the frequency of gall-bladder disease at all ages, though he says that 5 to 8 per cent. of women and 2 to 4 per cent. of men have gallstones after the age of fifty. Of 1224 women operated upon for uterine fibroids at St. Mary's from 1901 to 1910, $7\frac{1}{2}$ per cent. had gallstones.

Waterhouse⁴ believes that the majority of the fat, flatulent women seen at the clinics so constantly, without obtaining much relief, are really gallstone sufferers.

There is little doubt of the correctness of the theory that gallstones are produced through the action of attenuated bacteria which produce a desquamation of the epithelium of the gall-bladder, this serving as a nucleus upon which the cholesterin and other salts are deposited. Bacmeister⁵ holds that simple stagnation of the bile, *per se*, may cause cholesterin to crystallize out and build up one or more stones by radial formation without previous inflammatory processes being present. But, he says that after the stone is formed it may produce irritative inflammation.

Moynihah⁶ has described a condition in which fine grains of calculous material are embedded in the mucosa. The wall of the gall-bladder may appear normal, being thin and pliable. Particles of the grit are also found in the bile, but no stones.

Why cholecystitis should develop in some individuals and not in others cannot be fully explained at present. Bacteria in health can be, and are, excreted through the gall-bladder. Some conditions must be present favorable to their development in the gall-bladder. How does excessive intestinal putrefaction influence the production of cholecystitis? Is it because of an increased number of bacteria carried by the portal vein to the liver in this condition? Why do gallstones and obesity so often come together? How is it that cholecystitis occurs so frequently in pregnancy and that a preëxisting stone often ceases to be quiescent at that time? These and other questions can only be answered tentatively. The influence of sedentary life and overeating is somewhat easier to explain.

A cholecystitis is probably nearly always present before stone formation, but after the appearance of the stone each condition is made worse by the other. The early symptoms are due to the inflammation whether a stone is present or not.

Gall-bladder disease is a hard malady to diagnosticate, hardest in the first stages before stones have formed and in the cases where a mild catarrhal process has continued for years without producing colic or jaundice. Such a condition may persist for two to six years or even longer. Stones tend to stay in the bladder. After colic has occurred or jaundice is present the diagnosis is easy,

⁴ Lancet, May 8, 1909.

⁶ Annals of Surgery, December, 1909.

⁵ Münch. med. Woch., May 11, 1909.

but much valuable time has been lost and cases should not be allowed to progress thus far. Later the diagnosis again often becomes difficult if frank colics have ceased and the symptoms are due to the results of a previous cholecystitis and stone, adhesions, etc., as expressed by Morris—"cobwebs in the attic of the abdomen."

Until a few years ago cholecystitis or gallstones were not diagnosed until the occurrence of colic or jaundice, symptoms of complications which render all treatment more difficult. Now, early cases are recognized, most often by the specialists and the surgeons to whom, principally, is due the credit for our understanding of the symptoms during the first stages, previously "innocent gallstones."

As before mentioned, the writer is not in accord with the expressions of a number of those who claim that the early diagnosis of cholecystitis is easy. It is difficult. Mayo states that questioning those in whom gallstones were found at operation for other troubles practically always resulted in obtaining a history of the earlier symptoms of gallstone dyspepsia. However, it is decidedly easier after we know a condition is present to obtain a satisfactory corroborative history than it is to make such a diagnosis before. Another point, in the average patient it is next to impossible to obtain an accurate history of the beginning of a mild chronic trouble of slow progress. Patients have either paid little attention to the mild dyspeptic symptoms or have forgotten what impressed them at the time.

We are told that the gall-bladder has its own type of digestive disturbance (Coleman). To this I can hardly subscribe. The dyspepsia of cholecystitis more often than otherwise is not characteristic. The most that we can say is that some of the symptoms are decidedly suggestive, and, if we can rule out disease of the stomach and appendix, or, if we can find tenderness over the gall-bladder, then we can be more certain. Some writers differ entirely in describing certain symptoms, as for instance the time of occurrence of pain and the effect of food.

I shall mention some of the symptoms of mild cholecystitis or gall-bladder dyspepsia as advanced by different observers. Moynihan's "inaugural symptoms" are slight pain, not severe, but a discomfort, most often in the epigastrium, but not well localized; uneasiness; flatulence; ill-defined sensation of tightness; weight and oppression generally referred to the stomach after meals; which is usually relieved by belching; more severe pain which may radiate to the right shoulder. He describes a feeling of coldness and a slight shivering, and again a sudden short catch in the breath. Still other symptoms are drowsiness, inability to concentrate the mind and a sense of weight and fulness in the head. His confirmatory signs are tenderness on deep inspiration to thumb pressure

under the edge of the ribs, or dorsal tenderness and skin hyperesthesia over the area corresponding to the gall-bladder zone, the eleventh dorsal vertebra to the first lumbar and from one inch to the right of the spine to the posterior axillary line.

The above symptoms may come on at night together with palpitation of the heart. Here it may be noted that Babcock⁷ has reported 13 cases in which myocarditis was so severe that the gall-bladder trouble was entirely overshadowed by the heart symptoms. Others also have noted the marked heart symptoms.

Graham, quoted by Coleman,⁸ distinguishes four stages in the development and symptomatology of gall-bladder disease. In the first stage there are symptoms of mild disease of the stomach, irregular attacks of indigestion accompanied by gas formation and a feeling of epigastric constriction or tightness. There is discomfort, sudden in onset and frequently accompanied by chilliness, belching, regurgitation or vomiting. The chief characteristics of these attacks are their suddenness, irregularity and mildness. In the second stage pain occurs which may be dull or more severe and is located under the right costal arch. It may be aggravated by food, sudden exertion or deep inspiration. The attacks are evanescent in type and on their disappearance the patient enters upon a period of good health. The third stage is that of typical gallstone colic. Here the diagnosis is easy. The surgeon sees the majority of patients first in this stage. The fourth stage represents chronic gall-bladder disease with complications of adhesions, obstructions of the common duct, pancreatitis, cancer, etc. In this connection I may remark that pancreatitis sometimes appears before the fourth stage is reached. I have had one patient exhibit symptoms of beginning pancreatitis before she had experienced a single attack of real colic and another has had but one attack which was unaccompanied by obstruction or jaundice.

Sherren,⁹ basing his report on 43 patients with gallstones, considers the special points in the dyspepsia due to biliary trouble to be the associated flatulent distention, the frequency with which the patient is awakened at night, the non-relief of pain by taking food, and the relief by vomiting if this should occur, though it is unusual. He says that abdominal examination may settle the matter, as there may be a distended gall-bladder which may be felt or a slight tenderness under the right lower ribs may be present.

Wm. J. Mayo, in speaking of cholecystitis without stones, says that there is usually an habitual tenderness in the region of the gall-bladder. He says that as a rule colic is not a prominent symptom and, if present, is not as severe in character as that accompanying stones. He speaks of the presence of mild constitutional symptoms, lassitude, and other signs of mild toxemia, there being some-

⁷ Jour. Amer. Med. Assoc., lvi, 887.

⁸ Lancet, April 1, 1911.

⁹ Ibid., lii, 1904.

times for months a slight evening temperature without loss of weight. He describes the two most frequent forms of non-calculous cholecystitis as (1) a distended thin-walled gall-bladder containing several ounces of colon-infected bile, often of foul odor; (2) a gall-bladder with walls much thickened and white, often containing a thick, tarry material.

Whenever I see a stout woman, around or past middle age, with dyspeptic symptoms I think of gall-bladder disease and do not dismiss it from my mind until I am certain that her symptoms are due to other causes. A previous history of typhoid is significant. The points upon which I would lay particular stress are the following: Mild dyspeptic symptoms which are neither constant nor periodic, but appear suddenly at irregular intervals and disappear in like manner; the absence of a gross dietary indiscretion or if an attack has followed eating of some indigestible substance, as is sometimes the case, the absence of attempts on the part of the stomach and intestines to rid themselves of the offending substance by vomiting or purging; the presence of considerable flatulence; discomfort or mild pain not strictly localized, but confined to the upper part of the abdomen; the frequent appearance of this pain at night; and often a subicteric hue to the skin. These are the most characteristic symptoms of gall-bladder dyspepsia, but I do not feel warranted in making a diagnosis until I can obtain some tenderness in the gall-bladder region or perhaps only a fleeting rigidity of the right rectus, and until I have thoroughly examined the urine, stomach contents and feces to rule out other conditions. Some reflex disturbance will actually be found in the stomach of a number of patients. Lichty after gastric analyses in 156 gallstone patients deduced the fact that 75 per cent. of all gallstone cases have secretory disturbance and two-thirds of these have hypersecretion. Disturbances of motility exist in nearly the same proportion.

I have thought that an aid to the diagnosis of pathological changes in the bile might be found in the use of the Einhorn duodenal pump and the aspiration from the duodenum of either of the two sorts of bile described by Mayo as occurring in this condition, but as yet I have not had occasion to try this.

I have purposely spoken of the diagnosis of cholecystitis and not of cholelithiasis since the latter diagnosis cannot be made in the absence of colic. It should be stated that inflammation of the gall-bladder is present and probably one or more stones. Kehr, after performing 1668 gallstone operations says that only in exceptional instances is it possible to state positively the presence of gallstones.

The conditions described by various observers, which must be differentiated from cholecystitis, may be briefly mentioned and comprise, gastric and duodenal ulcer, cancer, intestinal colic, gastric neuroses, reflex disturbances from chronic appendicitis,

crises of locomotor ataxia, etc. A rare but extremely hard condition to differentiate is chronic gastromesenteric ileus. I saw such a case with Drs. Morgan and Clark. The patient's trouble had been diagnosticated by others and by us as either ulcer of the stomach or gall-bladder disease. Operation disclosed nothing but a dilated stomach and first part of the duodenum due to gastromesenteric ileus. A gastro-enterostomy has completely relieved her.

In discussing the treatment of gall-bladder dyspepsia or cholecystitis I shall confine myself to the medical side. Some there are who believe that the only medical cases are those in whom an operation is not feasible. This is the view held most frequently by American and English surgeons. They believe that patients should be operated upon as soon as the diagnosis can be made, before complications occur to render operation more difficult. Deaver, however, says that it is impossible to differentiate a stone-forming biliary catarrh from any other biliary catarrh, so it is necessary to wait until stones are actually formed before we have a basis for operation. German surgeons also are slower to operate. Kehr¹⁰ claims that operative treatment is required more for the infectious processes and to prevent their spread to other organs than to remove the stones themselves.

There can be little doubt that cholecystostomy, or even cholecystectomy, is indicated in a number of cases, particularly long-standing cases and those of considerable severity, often accompanied by complications. Also there can be little doubt but that drainage will help or cure all cases including the earliest, whether stones have already formed or not. However, no one is anxious for unnecessary operations, and if it can be shown that in certain patients the removal of the infectious processes can be secured by other means operation would not be favored in these instances. This I will endeavor to do.

Kolisch,¹¹ after years of experience, is convinced that dietetic measures are probably the most important of all in the treatment of gall-bladder disease. His aim is not to attack the stone, if one be present, but to combat the inflammation in the gall-bladder. Treatment should aim to avert anything liable to further injure the already weak biliary functions, and diet should be arranged to spare the liver as much as possible and keep the intestines in good order and free from catarrhal processes. He ascribes the good effect of Carlsbad water to its effect on the intestines. The diet should contain no chemical, thermal, or mechanical irritant. There should be no overeating. Particularly to be avoided are condiments, spices, acids, raw vegetables, and fruits, fats which do not melt readily, fat and salted meats, foods prepared with yeast or fermentation, cold drinks, much albumin with extractives and

¹⁰ Münch. med. Woch., March 21, 1911.

¹¹ Medizinische Klinik, April, 1910.

purins. He advocates in conjunction with the diet abstinence from rough sports for at least a year and claims as a reward permanent latency of the gall-bladder disease.

My own treatment for all early cases and mild cases, which I have used with good results even in some cases that had had attacks of real colic is something like that of Kolisch, but with added features which I think make it somewhat more reliable.

The patient is told to take, on awakening, one to two glasses of warm Carlsbad water, after which to turn on the right side for twenty minutes. On arising, if conditions do not contraindicate at the time, a few selected mild abdominal exercises are to be performed followed by a cold towel bath while standing in warm water. The brisk rubbing is followed by a glowing cutaneous circulatory reaction.

The diet is regulated so that there shall be no overeating and no irritation. It should be a well-balanced diet with, however, a preponderance of cereals and vegetables. The same things are forbidden as by Kolisch and, in addition, a still further reduction of fats. Even the more easily digested fats, as butter, olive oil, and cream, are minimized. In order that constipation may not result or be aggravated by the small amount of fat I order at bedtime 2 or 3 tablespoonfuls of albolene. This acts as a lubricant, is not digested or absorbed and is excreted from the body in the same form in which it is ingested. Albumins are considerably reduced in order to minimize intestinal putrefaction which is nearly always manifest. If a somewhat low caloric value is attained in the diet at first I consider it an advantage, rather than otherwise, if the patient is stout.

Medicinal agents calculated to reduce the inflammation in the gall-bladder, antisepticize the bile and render it more fluid, are hexamethylenamin administered several times a day up to a total of 30 grains in twenty-four hours, and bile salts 5 grains three times a day. Later both the remedies may be cut down to a smaller amount and continued for a considerable length of time. If signs of a relapse appear the doses may be temporarily increased. At the beginning of treatment if the inflammation is subacute hot poultices and complete rest in bed for several days are indicated.

I cannot speak authoritatively as yet as to the permanency of the results of this treatment, but I have so far no reason to regard it with anything but confidence and, at least, worthy of a trial before operative measures are undertaken. I know that the inflammation rapidly subsides and the patient feels much better almost from the start. Again, I feel that if operation is performed this treatment will render convalescence shorter and cure more certain. Recurrence after operation is not so infrequent but that it is well to take precautions.

Several cases will illustrate the symptomatology of gall-bladder dyspepsia and the rapid subsidence of symptoms under treatment.

Mrs. M. A. T., white, aged sixty-nine years, married, seven children. Past history negative. Present illness dated back for thirty years, coming in attacks, perhaps once a month. For the last ten years she had been free from them. There was a return of the trouble the month before she consulted me. During that month she had three attacks. Her attacks consisted of pain in the pit of the stomach and at times over the gall-bladder. When severe they radiated to the back and right shoulder. She was always puffed out with gas at the time and just before the attack would belch considerably. There was considerable nausea but rarely vomiting. Her bowels were generally constipated.

Physical examination disclosed everything normal except the following: Belly large and pendulous, panniculus abundant, and recti somewhat relaxed. Moderate tenderness under right costal border but gall-bladder not palpable. Slight tenderness across the mid-epigastrium becoming less on the left side. This corresponded with the position of the pancreas. Weight was 249 pounds; hemoglobin, 85 per cent.; blood pressure, 160 mm. A diagnosis was made of gall-bladder disease. She probably had a stone at first, which was passed, as it is inconceivable that it should remain latent for ten years when attacks had been so frequent before. At the time of examination she was just recovering from one of the attacks. No jaundice had been evident. The tenderness over the pancreas without doubt indicated a low grade of inflammation in that organ. After four days of treatment all gall-bladder and pancreatic tenderness had completely disappeared and she felt perfectly well. While she has had one attack, mild in nature since, it was when she lapsed in her treatment and she has had no symptoms for the last three months.

Mrs. E. G., white, married, three children, aged thirty years. Referred to me by Dr. R. R. Walker. Family and past history were negative. She began to have "stomach trouble" seven years ago and for the two years before consulting me was much worse. During this time she gained in weight. The trouble would come in attacks at irregular intervals, toward the last coming oftener and being more severe. Her symptoms were discomfort in the epigastrium, nausea, occasional vomiting, bloating, and a feeling of flatulence, a good deal of belching and heartburn between attacks. Her pain was also often in the gall-bladder region and would at times radiate to the shoulder. It was not dependent on food and would frequently come on during the night. Her bowels were irregular.

Examination showed a stout healthy looking woman, with good color in her cheeks but a subicteric hue to the skin. The scleræ were decidedly bile tinged, but she had never had real jaundice.

All organs were normal save the following: There was a spot of moderate tenderness in the mid-epigastrium, just below the xiphoid, also, in the gall-bladder region and extending across the upper abdomen to the left side, over the pancreas. The urine showed the faintest trace of albumin and a slight excess of indican. The strong benzidine reaction for occult blood in the stool when on regular diet disappeared after a meat-free diet. The thread test for ulcer was also negative, so this condition was ruled out. A diagnosis was made of gall-bladder disease and slight pancreatitis. Five days after beginning treatment she felt and looked well. The tenderness and other symptoms had completely disappeared and she has had no further trouble in the last six months except for a slight spell while away from the city and not taking care of herself.

I shall mention the case of Mrs. F. because her condition was more acute with slight fever and a leukocytosis of 15,400. Her symptoms were about the same as those of the above mentioned patients, but more pronounced. She, also, has been doing satisfactorily. In beginning treatment in her case rest and the icebag were used for several days.

In cases of acute cholecystitis of severe type operation should be performed without delay. I would not have it understood that I favor trying this medical treatment in any case where there is danger in putting off operation.

In closing I would emphasize the following conclusions:

1. There are numbers of dyspeptics whose symptoms are due to gall-bladder disease.
2. Diagnosis should be made early and treatment instituted before the occurrence of gallstones if possible.
3. Surgery is the only treatment for a certain class of cases.
4. In all early cases, exclusive of those dangerously acute, medical treatment, according to the principles outlined above, should be tried before recourse to surgery.
5. In a number an apparent cure will be effected, particularly if no stones have formed and it is usually impossible to state whether or not stones are present.
6. The medical treatment can do no harm in those patients who have not yet had symptoms of obstruction.
7. If two attacks occur after treatment has been started there is still time for surgery, and an operation should then be performed. It is not advisable to give medical treatment further trials.
8. In those cases which do finally come to operation the previous treatment will usually have put the patient in a better condition.
9. The foregoing diet and medication should also be given in the post-operative treatment of those who require surgical intervention.

THE VALUE OF FROZEN SECTIONS IN THE TEACHING OF PHYSICAL DIAGNOSIS.¹

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THE thought of employing frozen sections in the teaching of physical diagnosis had its inception some three years ago. At that time, the writers were investigating the causation of the hydrothorax resulting from chronic valvular heart disease. Some of the bodies used for this study happened to be those of individuals who had died from pulmonary tuberculosis. In studying these sections it became apparent that by their use the gap which had hitherto existed between the pathological specimens and the interpretation of the signs produced by such a lesion in the living subject could easily be bridged. The method usually followed in teaching physical diagnosis is to demonstrate on the living subject certain physical signs, the teacher then stating, or indicating by diagrams that such and such signs indicate such and such a condition. In the instances in which it is possible for the student to see the pathological specimens from a case studied during life, much of the value is lost, because of the dissociation of the organ from its anatomic surroundings, and also, in the case of the lungs, by their collapse.

Up to a comparatively recent time, the study of anatomic relationships and minutiae was based entirely on dissections of soft bodies. Under this system of learning anatomy it was impossible to get an *x-ray* conception of any given area of, for example, the chest. One could know what lay *immediately* under certain ribs, but when a through and through conception was desired it could be only approximately accurate, this being true of both the thorax and the abdomen, but especially of the former. The introduction of freezing and sectioning of cadavers has added to the accuracy of our conceptions, but this method, while valuable for study purposes, is open to the objection that the specimens lack permanence, and are, therefore, unfit for repeated demonstrations. Now that we have

¹ Read before the Section on General Medicine of the College of Physicians of Philadelphia, November 27, 1911.

a means of preparing and preserving our material by the use of formalin and freezing, our specimens are available for repeated study and indefinite use.

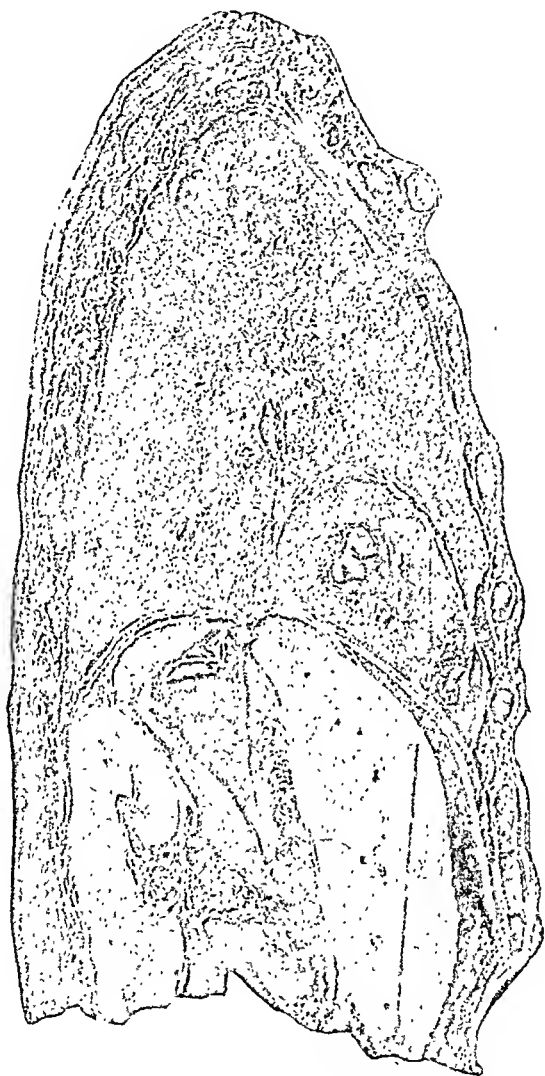


FIG. 1—Sagittal section through left apex. This section shows a posterior cavity with the remainder of the apex practically normal. The physical signs in front would be obscured by the almost normal tissue.

The art of diagnosis is, after all, the art of visualization, and in order to visualize the abnormal, a thorough ability to mentally picture the normal is essential. The groundwork of accurate diagnosis is a keen knowledge of the anatomy of the parts concerned, and the diagnostic work of a clinician can never surpass in accuracy his knowledge of the normal anatomy of the parts dealt with. While

it may be true that ultra-minute correctness in diagnosing lesions is not necessary in, for instance, tuberculosis, in order to treat a given case correctly, still the aim of the teacher should be to impress the necessity for such correctness upon the students under his tutelage.

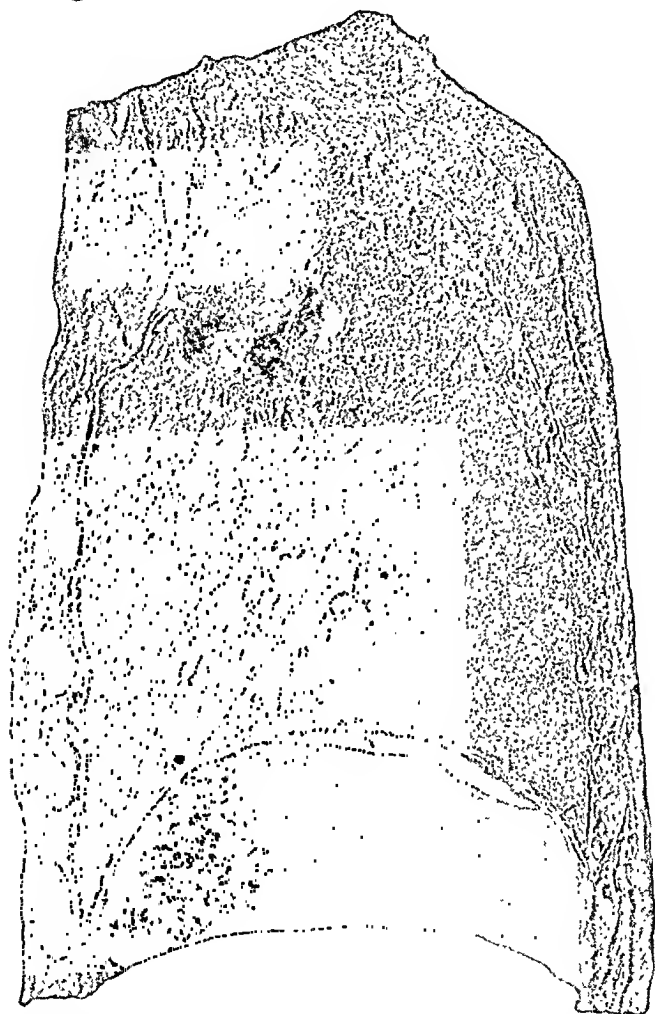


FIG. 2.—Sagittal section through right apex. This section shows a subpleural anterior cavity with densely infiltrated tissue below and in front. The physical signs would be most marked above and below the clavicle. The distance from the suprascapular fossa to the cavity should be noted.

One trouble in teaching the diagnosis of chest conditions is that the student comes up to that point in his undergraduate career with an anatomic knowledge largely of a descriptive character. He has acquired it by lectures and in the dissecting room, has traced the pulmonary artery into the lungs, the pulmonary veins into the heart, has seen the trachea and bronchi, has learned the order of vein, artery, and bronchus from above downward, and from before backward, and has collected other semi-useless bits of

anatomic A, B, C. But what conception does he have from personal observation of the real shape of the pulmonary apices, or of that of the chambers of the heart? What does he know of the difference between the depth of the thorax, from sternum to vertebræ, and that from nipple directly backward to rib? What true

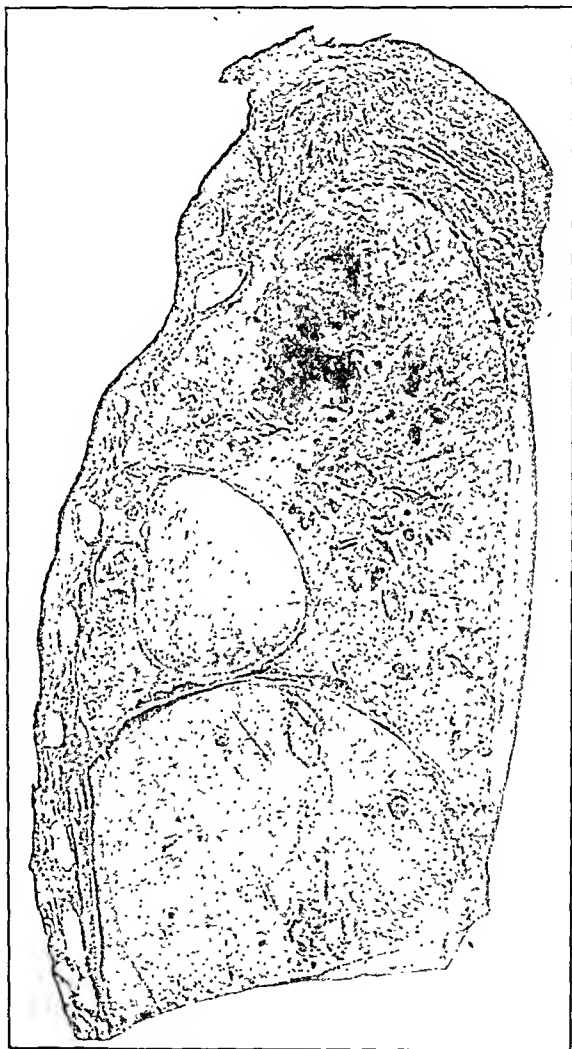


FIG. 3.—Sagittal section through right apex. This section shows ragged communicating cavities with dense infiltration of the lower lobe. The physical signs would be given both in front and behind. The distance from the supraspinous fossa to the cavity should be noted.

idea can he have of the amount of lung that lies posterior to the anterior facies of the vertebral column? How can he know of the difference in thickness of muscle and bone between the posterior aspect of the pulmonary apex and the surface, and that between the anterior aspect and the surface? How can he have any con-

ception of the mediastinal relations of the lungs, since in order to see them he has to destroy them?

The teaching of physical signs is open to the same criticism. The instruction is either abstract, dealing with variations in the percussion note and breath sounds, or if the living body is used to demonstrate these changes, the student is working with the chest wall interposed between him and the lesion being investigated. He is required to exercise his imagination without anything (except possibly diagrams) to aid him. The tremendous gap between the physical signs on the one hand and the lesion being studied on the other is entirely unbridged. As we already have pointed out, the only aids hitherto afforded have been diagrams, and the teacher's say-so.

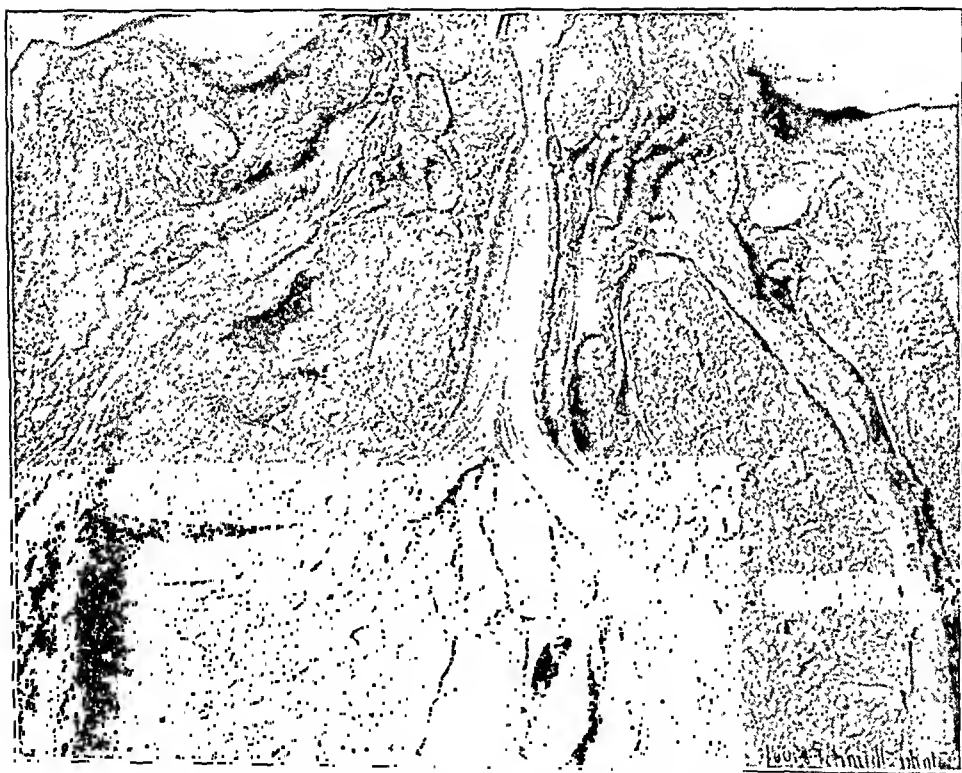


FIG. 4.—Frontal section in the axis of the trachea. This section shows the inclination to the right of the trachea, the relation of the right and left apices to the trachea, and the distance of the cavity in the right upper lobe from the top of the shoulder.

The study of living pathology is, of course, the ideal way to acquire knowledge of gross lesions. The next best method is to have our specimens of dead pathology as near as possible in the conditions present during life. The ravages of advanced tuberculosis can be well shown a student by placing before him a lung which is badly diseased, but this is all that can be shown.

Our experience has convinced us that the use of hardened sections

has filled this hiatus most satisfactorily. It cannot be denied that it is preferable to work from the known to the unknown, rather than the reverse, as is usually done. Applying this to the question

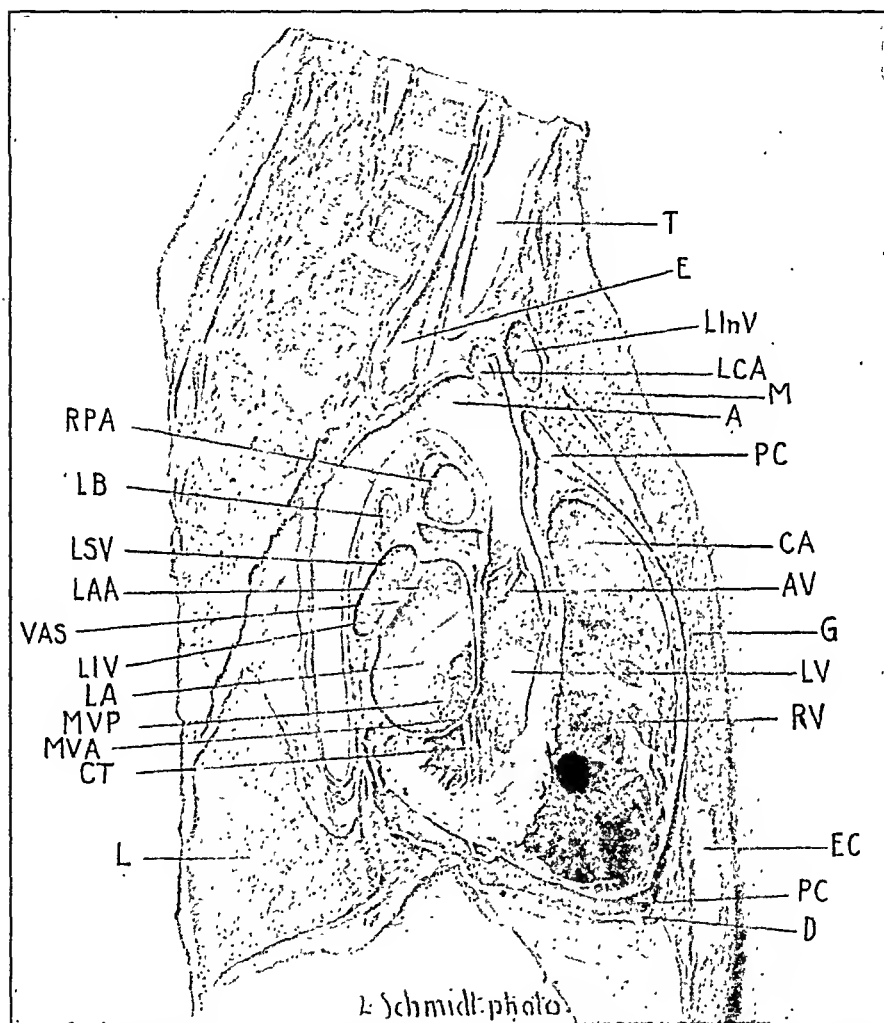


FIG. 5.—Sagittal section in the median line. This section shows the almost directly backward course of the aorta, the relation from before backward of the right ventricle, left ventricle, and left auricle, the relation of the aortic and anterior mitral leaflets, etc.: *L*, lung; *CT*, chordae tendineae; *MVA*, mitral valve, anterior leaflet; *MVP*, mitral valve, posterior leaflet; *LA*, left auricle; *LIV*, left inferior pulmonary vein; *VAS*, veno-appendicular septum; *LAA*, left auricular appendix; *LSV*, left superior pulmonary vein; *LB*, left bronchus; *RPA*, right pulmonary artery; *T*, trachea; *E*, esophagus; *LInV*, left innominate vein; *LCA*, left common carotid artery; *M*, manubrium; *A*, aorta; *PC*, pericardial chamber; *CA*, conus arteriosus; *AV*, aortic valve leaflets; *G*, gladiolus; *LV*, left ventricle; *RV*, right ventricle; *EC*, ensiform cartilage; *D*, diaphragm.

under discussion it would seem far more rational to show the student a section of a tuberculous lung *in situ*, and indicate what physical signs must necessarily be produced from such a lesion,

than to demonstrate a chest *in vivo*, and tell him what the signs indicate.

In teaching students the physical signs of tuberculosis at the Phipps Institute of the University of Pennsylvania, the following procedure is employed. They first examine a series of extracted



FIG. 6.—Frontal section. This section shows the distance from the supraspinous fossæ to the apices, the lower pulmonary lobes comprising the greater part of the posterior lung space, the contact of the left lung with the thoracic aorta, and the relation of the right base to the liver and the left base to the stomach.

lungs, preserved by the Keiserling method. These specimens show practically every change from that of a small cluster of tubercles, illustrating an incipient lesion, to the most destructive ravages of advanced disease. The student is then shown the hardened sections, and has an opportunity to see the cavity in relation

to the ribs, clavicle, scapula, and soft parts, and according as the cavity is small or large, anterior or posterior, and covered by a thick or thin pleura, he can be taught at once what physical signs should be produced.

The next step is to assign a case for examination, and having seen a diseased lung *in situ*, he is well equipped to form a mental picture from the physical signs. Finally, after he has charted his findings they are censored by one of the instructors, and if any point is not clear, recourse is again had to the hardened preparations. And if a library of such specimens of sufficient variety can be collected to be shown concurrently with living cases, it will form a great aid in teaching the student to visualize the diseased conditions which come under his observation.

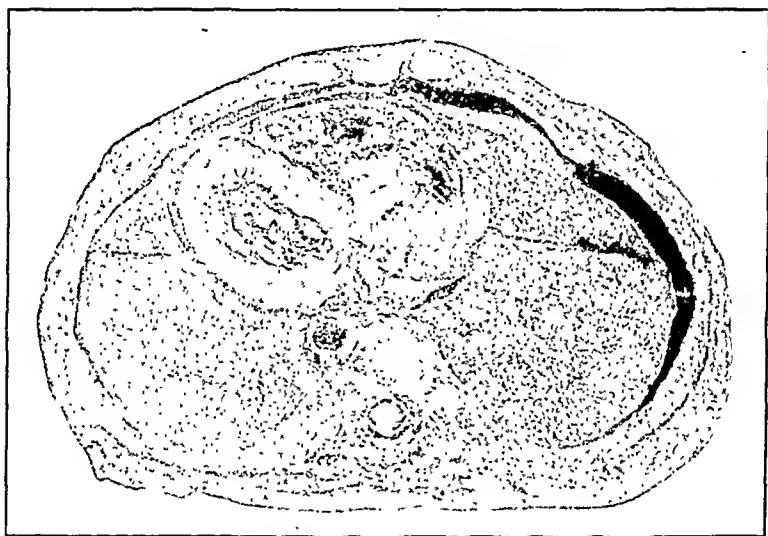


FIG. 7.—Horizontal section of child's thorax. This section shows the encroachment of the vertebral column on the intrathoracic space, the amount of space occupied posteriorly by the upper lobes, and the large area occupied by the heart.

To one who has never seen sections of the hardened thorax the obviousness of the essential facts of anatomico-clinical importance is most instructive. Among them may be enumerated the anterior, superior, posterior, and mediastinal relations of the pulmonary apices; the apposition of the right upper lobe to the trachea; the inclination to the right of the trachea; the almost directly backward course of the aortic arch; the proximity of the right base to the liver on the one hand, and of the left base to the stomach on the other; the amount of costophrenic pleural space unoccupied by the lung. In addition, there can be shown the tremendous encroachment of the vertebral column on the intra-thoracic space; the thickness of the muscles overlying the spine (and incidentally indicating the limitations of spinal percussion); the distance of the

bronchial lymph nodes from both the anterior and posterior aspects of the thorax. Innumerable points of interest are shown in regard to the heart, for instance, the posterior position of the left auricle, in relation to all the other cavities, even including the right auricle; the distance from the surface of the various valves; the relation of the aortic valve to the infundibulum, etc.

The preparation of the specimens is a comparatively simple matter. The bodies are given an arterial injection of 15 per cent. formaldehyde solution, and put in cold storage until they are frozen solid. They are then cut with an ordinary carpenter's hand-saw. As regards the plane of sections, we have been guided by the following principles: For study of the lungs, sagittal sections are the best; for the air passages, a frontal section in the axis of the trachea is of most value; to demonstrate the relations of the pulmonary bases, the frontal plane is of greatest usefulness; to show the heart to best advantage, sagittal sections are given the preference; for the superior mediastinum, horizontal and sagittal sections are of about equal value.

We have also used ordinary dissections of these hardened bodies. They are not difficult to handle, and they have the great advantage of not collapsing and of retaining their shape indefinitely.

THE TREATMENT OF PULMONARY TUBERCULOSIS BY COMPRESSION OF THE LUNG.

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SINCE 1825 the desirability of restricting the expansion of the tuberculous lung, and of approximating the walls of cavities, has been strongly felt by many of the best minds in the profession, and vague, inconsequent efforts have been made to accomplish these results. Carson,¹ of Edinburgh, suggested puncturing the costal pleura in order to transmit atmospheric pressure and so compress tuberculous cavities. Piorry² tried tightly strapping the thorax and putting a heavy weight over the cavity in order to keep the chest wall quiet, and maintained that he had seen marked improvement follow. Many distinguished clinicians have reported unexpected recoveries in pulmonary tuberculosis after the occurrence of a pleural effusion, or a pneumothorax. *A priori*, it is easy to understand how anything occupying space in the pleural cavity, will proportionately reduce the size of the lung, and cripple its

¹ Canstatt: Pathologie und Therapie, Erlangen-Enke, 1843.

² *Ibid.*

power to expand. Today it is evident that by filling the pleural cavity with gas, the lung may be reduced to its smallest possible compass, the walls of ulcers and cavities closely approximated, and held so, almost as immovable as in a vise.

This simple, almost selfevident, fundamental principle escaped the attention of the medical profession until 1882, when it was crystallized out of the mass of vague, generally felt, impressions, by Forlanini,³ of Pavia, who suggested filling the pleural cavity with a gas in order to immobilize the lung and prevent its expansion. In 1894, Forlanini⁴ reported a case successfully treated by this method. In 1898, Murphy,⁵ influenced by the desire to defunctionalize the lung, independently conceived the idea of compressing it by filling the pleural cavity with nitrogen, and published a report of 5 cases treated by this method. The next year, 1899, his assistant, Lemke,⁶ reported 53 cases. Unfortunately Lemke died, and Murphy, although repeatedly urged to use the method, and fully convinced of its scientific value, persistently refused to do so because it would take him out of surgery into medicine. In 1905, 1906, and 1907, Forlanini's⁷ reports attracted the attention of Brauer, now Chief of the great Eppendorfer Institute in Hamburg. This eminent investigator became thoroughly convinced of the value of the method and soon Lucius Spengler, and Ludwig von Muralt, of Davos, were associated with him in its use. They were followed by some of the most eminent specialists in Europe, and at present some 400 cases have been reported, so that sufficient data has been accumulated to furnish material for a critical estimate of the value of compression of the lung by means of nitrogen injections into the pleural cavities in the treatment of tuberculosis. These reports show that the method is not applicable to all cases because of pleural adhesions and pleural neoplasms, but that when it can be used, and the lung is compressed completely, and kept so for a sufficient length of time, recovery has invariably followed.

As a rule, compression of the lung by means of an artificially produced pneumothorax has only been attempted in otherwise hopeless cases. It has been universally assumed that this should not be tried until all else has failed. When the whole of one lung and occasionally part of the other had become involved it was felt that the gravity of the condition justified the seriousness of the procedure. Therefore, the cases reported are practically all of a hopeless, desperate nature. Many cases recovered, others succumbed, but in all cases, failure was due, not to the use of the

³ *Gazzetta degli Ospedali*, August, September, October, November, 1882.

⁴ *Münch. med. Woch.*, 1894, No. 15; *Gazzetta medica di Torino*, 1894, Nr. 20 e 21; 17 e 24 Maggio.

⁵ *Oration on Surgery*, *Jour. Amer. Med. Assoc.*, 1898.

⁶ *Jour. Amer. Med. Assoc.*, 1899.

⁷ *Gazzetta medica di Torino*, 1895, Nr. 44; *Deutsch. med. Woch.*, 1906, Nr. 35; *Gazzetta med. Italiana*, 1907, 1908.

method, but to inability to employ it properly because of complications. For example, if the lung is held fixed by dense pleural adhesions it cannot be compressed. If the pleural neoplasms are too hemorrhagic it is difficult to enter the pleural cavity. Renal or intestinal lesions may be aggravated by the pressure, and other serious complications, such as diabetes or incompetency of the heart, contraindicate attempts at compression.

If a patient with pulmonary tuberculosis is doing badly in spite of climate, nursing, and medical skill, what then remains? If, after months of absolute rest combined with every advantage and aid that can be procured, the process steadily advances, and more and more of the lung becomes involved, what shall we do? Why should we not check this extension of the disease by actively compressing the affected lung until the fluids and decomposing masses are driven out of the lung through the bronchial tubes; until the circulation is so suppressed that the lung becomes clean, firm, and dry; and a passive stasis so encourages an exuberant development of connective tissue that all the tuberculous lesions are converted into durable scars, and all signs of tuberculosis are completely obliterated?

The cases so far reported are practically of one type. The unsuccessful ones vary according to the nature of the cause of the failure. The successful ones are all much alike, and for the most part represent advanced and hopeless cases with one lung completely involved and often the apex of the other, usually with a history of years of unsuccessful attempts at recovery under the most favorable circumstances, and showing fever, night sweats, profuse, purulent, expectoration containing tubercle bacilli and elastic fibers, emaciation, and prostration.

When nitrogen is injected into the pleural cavity, and more and more pressure is obtained, the typical results are manifested in proportion to the degree of compression of the lung. At first the temperature may rise, the pulse quicken, and the amount of sputum increase because of the pressure, but when these first effects are over, the lessened production and absorption of toxins is shown by a fall in temperature and pulse rate, and diminished expectoration. With complete compression of the lung, the breath sounds disappear, or are heard only as a metallic whistling. There is a drum-like resonance over the entire side except over the shrunken lung, which the x-rays show has little or no ability to expand. All this is but preliminary. The enemy has merely been driven out. The real reconstructive processes must complete the work, so that recovery will be of the most durable and permanent nature, and no future relapses can occur. While the lung is compressed it is safe, for no infection can enter. It is a more difficult task to put the lung in such condition that it will not always have to be compressed, but may with entire safety to the patient re-expand and

resume its function. This is accomplished by maintaining sufficient pressure within the pleural cavity to hold the lung closely together so that the reparative processes may never be torn. Thus an opportunity is given for fibroblasts to shoot out from the walls of the injured bloodvessels, lymphatics, and bronchial tubes into the injured tissues and for cicatrizing processes to convert the walls

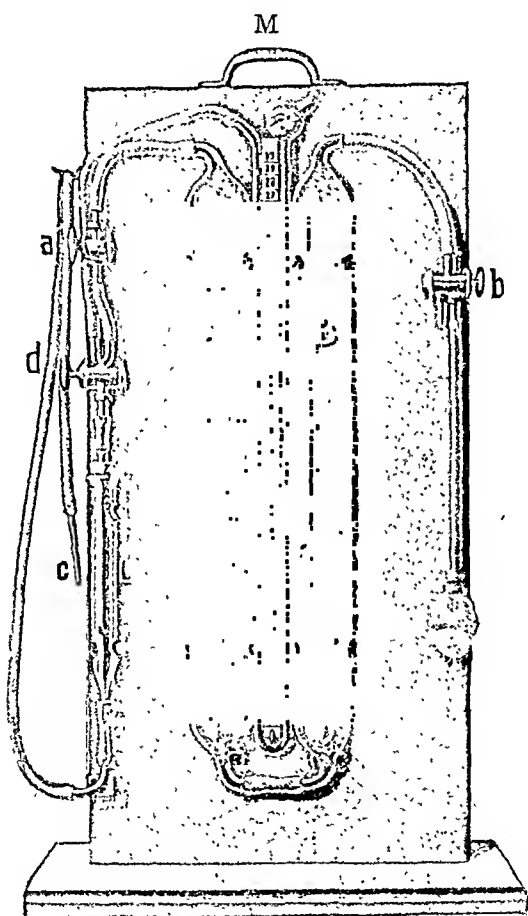


FIG. 1.—Forlanini's apparatus, modified by Saugman.

of ulcers and cavities into firm, durable scar tissue. Fortunately, this organizing invasion of fibroblasts does not concern itself with sound tissues. Elaborate experiments⁸ have proved conclusively that the sound portions of the lung are in no way affected by this process. Moreover, uninjured alveoli show no tendency to adhere

⁸ Brauer's Beitr. z. klin. Tuberkulose, Band xii, Heft 1; *ibid.*, Band x, Heft 3.

no matter how long the pressure has been kept up. After a year or more when the pressure is removed the healthy alveoli readily separate and resume their function.⁹

In order to insure complete anatomical recovery, it is generally agreed that the lung must be kept firmly compressed for about a year in uncomplicated cases before it is safe to allow it to expand. At first the nitrogen is injected frequently, then less often as the pleural surfaces lose their power of absorption. In the beginning the injections are made every other day, then twice a week, and later on once or twice a month will suffice.

The simplest and most portable apparatus for making nitrogen injections into the pleural cavity is that devised by Forlanini and modified by Saugman by the addition of a manometer (see Fig. 1). The apparatus is mounted upon a board, and consists of two cylinders, *A* and *B*, each holding about a liter, and connected at the bottom by rubber tubing. Between the two cylinders is a U-shaped water manometer (*M*) 50 to 60 centimeters long. The graduated cylinder *A* contains the nitrogen; the cylinder *B* is filled with an antiseptic solution; *d* is a three-way stopcock connecting the needle-tube *c* with *A*, or with the manometer *M*. When the needle tube is connected with *M*, the manometer indicates the intrathoracic pressure, and the respiratory excursions; when connected with *A*, the nitrogen escapes into the pleural cavity. *L* is a glass filter through which the nitrogen must pass both on entering and leaving the cylinder. There is another three-way stop cock, *b*, connected with a bulb. At present this apparatus must be imported.

Brauer¹⁰ modified Murphy's¹¹ apparatus by the addition of two manometers, one for water and one for mercury (see Fig. 2). This apparatus may be easily made by using a simple U-shaped water manometer with the two jars. The nitrogen jar *N* is filled with sublimate solution. The water jar *S* is lowered and the nitrogen turned on. The nitrogen is filtered through a glass tube packed with sterile cotton. The supply tube of the nitrogen jar is connected with a three-way stopcock *D* which will either permit the nitrogen to pass into the pleural cavity through the needle *P*, or transmit the interpleural pressure to the two manometers, *W* for water, and *Q* for mercury.

Before attempting to compress a lung, the functional capacity of the other lung and the effect that the increased respiratory demands will have upon it must be carefully estimated. It is not so much the extent, as it is the nature and location of the process

⁹ Brauer's Beitr. z. klin. Tuberkulose, Band xii, Heft 1, S. 49 to 154; Münch. med. Woch., 1906, Nr. 7; Therapie der Gegenwart, June, 1908; Deutsch. med. Woch., 1906, Nr. 17; Ueber Pneumothorax, Programm der Feier des Rektoratswechsels, Marburg, a/L.; Wien. Therap. Woch., 1908, Nr. 33, S. 454; Therap. Woch., 1908, Nr. 29.

¹⁰ Brauer's Beitr. z. klin. Tuberkulose, Band xv.

¹¹ Loc. cit.

in the second lung that will determine the advisability of attempting compression. One lung may be safely compressed when a much greater portion of the second lung is in an old, dry, cicatrized condition than if it is involved in a wet, pneumonic process, and apical lesions are not as dangerous as those situated centrally.

There are two sources of error likely to confuse us in estimating the condition of the second lung. The rales heard over it may be chiefly transmitted from the other lung and entirely disappear as soon as the latter is compressed. On the other hand, deep, central lesions, quite unsuspected at the beginning, may be so aggravated by the increased functional activity of the lung that it will be unwise to persist in the treatment.

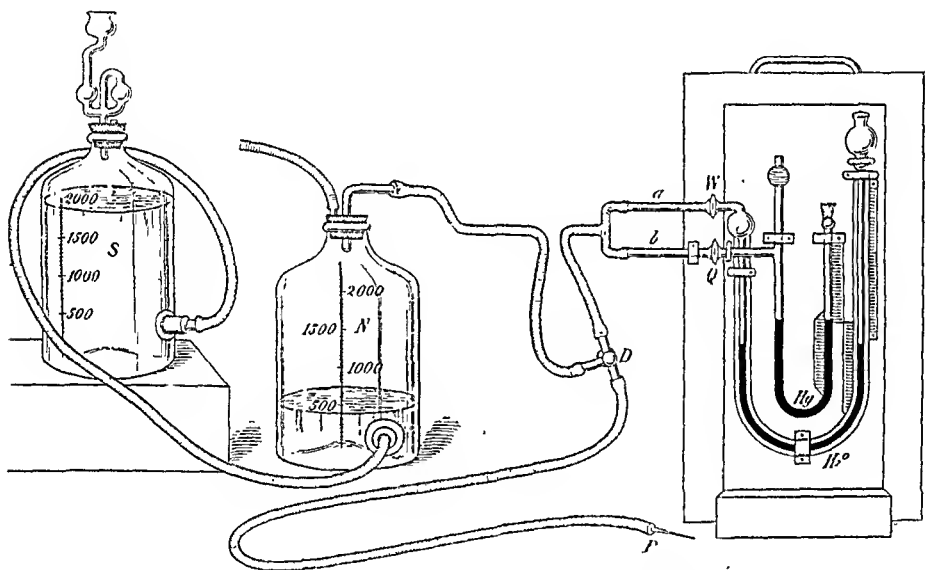


FIG. 2.—Brauer and Spengler's modification of Murphy's apparatus for nitrogen injections.

The technique of making nitrogen injections into the pleural cavity is as follows: Choose a spot for making the injection over an area where the breath sounds and resonance are best, in as wide an intercostal space as possible, avoiding the heart, the diaphragm, and the thicker muscles. Forlanini's method is to place the patient so that the selected site for injection comes uppermost, and arrange the arm so as to widen the intercostal space. Disinfect the skin with tincture of iodine and freeze with ethyl chloride. A fine hypodermoclysis needle may then be thrust through the chest wall until the pleura is felt to yield. Connect the needle with the manometer. If there are no excursions the needle is plugged or is in the lung or a bloodvessel. If for any reason the fine needle is not satisfactory, Murphy advises making a small incision just large enough to admit a medium-sized aspirating needle with a slightly

blunted point. As the pleura is felt to yield, air will be sucked through the head of the needle if there are no adhesions. If this sound is not heard the needle is either stopped up or is in the lung. The needle is then connected with the manometer, and if there are no excursions a new attempt must be made. The safest and most reliable method is that of Brauer, who makes an incision sufficiently long to afford a good inspection of the pleural surface after the tissues are retracted. If the pleura is glistening and smooth, and the motions of the lung are visible, he punctures the pleura with a blunt needle, carrying a fine catheter with which the pleural layers may be explored. When satisfied as to the existence of the pleural cavity, the needle is connected with the manometer. After the nitrogen has been injected, the incision must be closed by carefully suturing each layer of tissues. The after-fillings are made by using a fine needle without an incision.

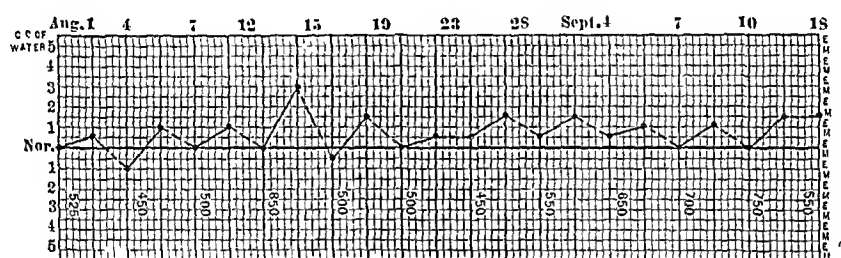


FIG. 3.—Typical curve of pressure within the pleural cavity following nitrogen injections.

The quantity and the frequency of the injections vary with each case. When there are no adhesions and the heart action is good, larger quantities at longer intervals may be given. If the heart is weak the pressure should be kept as low as possible and the injections given just often enough to maintain the standard desired. It may not be advisable to raise the pressure much until the heart is found to be equal to the task. When the patient is not incommoded by the pressure, 7 or 8 centimeters will not be too much. Each case is a law unto itself and the proper standard of pressure must be determined for each individual, and then maintained by giving the proper quantity at the right time (see Fig. 3).

The size and situation of the lung and the degree of compression is best shown by the *x*-rays. Failing this, the character of the breath sounds indicate the density of the lung, and the area of resonance the extent of the pneumothorax. As the lung becomes compressed, the rales and breath sounds give place to metallic breathing and, finally, to a sharp, metallic clinking, or the sound of a drop falling into a metallic space. When the lung is held out by adhesions, the breath sounds and rales persist over these areas, and metallic conditions are not induced. Bulging over the

previously shrunken side is frequently seen, and the difference in motility plainly felt.

When the pleural layers are held together by bands or adhesions, the clinical course of the treatment is altered, and the technique greatly increased in difficulty, so that we encounter all degrees of failure, from inability to produce a pneumothorax, to inability to compress the lung after it is produced. The dangers attending the method are also increased. Failure of the manometer to show typical respiratory excursions may be due to the inability of the pleural layers to sufficiently separate because of adhesions too near the point of puncture. A little nitrogen may aid in separating the pleural layers and produce perfect respiratory excursions. This is tempting, but dangerous, because without the manometer we have no idea where the point of the needle may be. If we do not have the respiratory excursions to guide us, we are unable to know whether the point of the needle is in the lung, or in a bloodvessel, or whether the needle is simply stopped up. If the pleuræ are adherent they are pierced as one and the needle goes on into the lung. In all probability a fine needle will not injure the lung unless it is moved about sufficiently carelessly to tear the lung tissue. If a large needle is used and the stiletto vigorously employed to ascertain the reason of the obstruction, the lung tissue may be considerably injured and death result from the formation of an abscess. If the wall of a pulmonary vessel is torn, air may be sucked in from the lung, or nitrogen may enter. The point of the needle may be in a bloodvessel, and the nitrogen enter the circulation directly. There is always the danger of embolism whenever a filling is made. Careful technique avoids the introduction of the nitrogen into the circulation, but there are two other theoretical dangers to be considered. It is quite possible that an angiomatous condition of the pleural vessels will cause the needle to tear one of the thin vessel walls without the needle becoming obstructed. Then as the nitrogen is injected it may be forced into the torn vessel. If there are clots in the pleural or pulmonary vessels, the pressure resulting from the filling may expel one into the circulation and thence to the brain. The cerebral phenomena of embolism are loss of consciousness, rolling of the eyeballs upward, contraction of the pupils or dilatation, loss of pupillary reflex, conjugate deviation, extension convulsions, trismus, instantaneous cessation of the circulation and respiration, or prolonged failure.

Very different are the phenomena due to insult to the pleura or the pneumogastric nerve, known as pleural reflexes. These vary from slight collapse or dyspnea to complete aphonia and spasm of the glottis. They are avoided by the preliminary use of morphine, whisky, by touching the surface of the pleura with cocaine, and by not using nitrogen below the body temperature. Insult to the pneumogastric nerves may cause paralysis of coughing and speech.

A peculiar source of difficulty and danger is found in an excessive development of the pleural circulation resulting almost in a neoplastic overgrowth. Under such circumstances it is difficult to introduce the needle into the pleural cavity without the needle becoming filled with blood, and even after a pleural cavity of some size has been created, we may fail in the attempt to find it.

If too much nitrogen is introduced under too high a pressure, the nitrogen may escape back through the track of entry and appear subcutaneously as an emphysema, or it may infiltrate beneath a muscle and lift it up. Instead of leaking out, the nitrogen may produce bulging of the unsupported anterior and posterior portions of the pleura with subsequent escape into the mediastinum, forming deep emphysemas, which crowd up into the neck or press against the heart causing alarm and distress to the patient.

My own experience with the method is far too recent to be conclusive, but the results obtained are so striking that I feel warranted in reporting them. In the cases in which I have thus far employed this method of treatment the indications for the operation were: Inability to arrest the process in 15 cases; inability to hold a previous recovery in 3 cases; impatience to return to work and unwillingness to risk the uncertainty of symptomatic treatment in 2 cases; while in another patient the operation was done on purely theoretical grounds; and 1 case was referred expressly for the treatment.

There were 3 deaths and 1 failure in the 15 cases, all of which were advanced and otherwise hopeless. One death was due to hemorrhage before the effects of the method could be obtained. This case was characterized by severe and persistent hemorrhages which were the indication for attempting the treatment. The second death was due to a violent exacerbation of an intestinal tuberculosis, together with an exaggerated course of tuberculin given after the patient left Highlands. The third left Highlands far too soon and was afterward not properly cared for. The case that did not improve still has a chance of recovery. She is gaining slowly and is in every way much better than before the attempt was made. The pleural cavity is filled with adhesions and there is an enormous, almost malignant development of the pleural collateral circulation. All of the others are doing well, and in all of them recovery could not have been made unaided.

Of the 3 cases unable to hold a recovery when made, 1 has been earning his living for over a year without the loss of a day's work, and the other 2 are in equally favorable condition.

There were 2 cases of business men impatient to resume work, and unwilling to risk the slow and uncertain results of symptomatic treatment. It is too soon to prophesy, but the lungs of both are being successfully compressed, and we have every reason to believe that within a year these men will return to work and be as free from the dread of a relapse as an anatomical recovery can make them.

A recovery after the removal of all foul matter and the complete suppression of all tuberculous activity, with their lesions converted into clean, strong scars, is a vastly different matter from the shutting-in process.

The theoretical case is one in which a tuberculous process is grafted upon an emphysematous lung. The heart, overburdened with athletics, alcohol, and tobacco, and stretched far to the right of the sternum, was unable to maintain a good pulmonary circulation. The lung was stiff with blood, the thorax rigid, the patient gasping for breath, and exhausted by the profuse expectoration consequent upon the vicarious development of the bronchial circulation. Arguing that collapse of the lung is fully as necessary as expansion, and that simply the separation of the pleuræ, thus allowing the lung to fall back a little from the chest wall, would give some support toward driving the blood out of the lung, we injected 200 c.c. of air and repeated this twice within two weeks. The relief was marked and persistent, the bronchial circulation is subsiding, the rales have disappeared, the temperature, previously 99° to 101°, is normal, the breath sounds are no longer wheezing, and the patient is much more comfortable and has no dyspnea.

The referred case is that of a young woman with an old inactive process in the right lung, and an active one in the left lung involving the upper two-thirds. The circumstances at the Sanatorium not being suitable for the patient, she was referred to one of the most scientific hospitals in the East, where the lung is being compressed with marked success.

A brief summary of some of the cases treated will best illustrate the results obtained by compression of the lung with nitrogen injected into the pleural cavity.

CASE I.—Schoolgirl, aged seventeen years; weight, 97 pounds. Illness of fourteen months' duration, characterized by periodic failure to menstruate and consequent exacerbation of cough, followed by vomiting and hemorrhages. The right lung was normal. The left lung showed in front, down to the fourth rib, and behind to the eighth rib, dullness and altered breath sounds. In the intervals of recovery the breath sounds were suppressed and expansion was uneven. During the failures to menstruate large and medium moist rales were heard over these areas. The sputum was full of tubercle bacilli. The indications for the operation were: Failure to hold a recovery after it was obtained; persistent hemorrhages; and inability to check the extension of the tuberculous process on account of the effects of vicarious menstruation.

The first injection of nitrogen into the pleural cavity was made on April 24, 1910, by Dr. Murphy, at the Mercy Hospital in Chicago. Nine-hundred cubic centimeters were first injected, and about the same amount was given twice within the next ten days. In the

first twenty-four hours the temperature rose to 103° , and the pulse to 120. There was a great deal of coughing and expectoration, and the patient could not lie down nor sleep. The following fillings gave little discomfort, and the return journey was much more easily made than the one to Chicago. The fillings were kept up at the Highlands Camp Sanatorium, and after two months the tubercle bacilli disappeared from the sputum. Today the patient is well and strong, has no cough, no expectoration, eats well, sleeps well, and her condition is in every way satisfactory. Since January, 1911, the fillings have been given by her home physician.

CASE II.—Lawyer, aged thirty-five years. The patient had moderate expectoration with an abundance of tubercle bacilli. He had been ill for two years, and was unable to build up by eating because of violent attacks of indigestion whenever any attempt was made to force the feeding. The left lung was normal throughout. The right lung did not reveal by physical signs the extent of the lesions because they were deep and central. The x-rays showed considerable infiltration in the middle and lower part of the upper lobe. For a year he made constant recoveries which he lost at every attempt to make physical efforts. Indications for compressing the lung were: The difficulty of healing central lesions; the inability of the patient to make or hold a recovery; and the necessity of supporting his family.

In August, 1910, an injection of 500 c.c. was made according to Murphy's method. There were no difficulties, and after the fillings had been kept up for two months the lung was thoroughly compressed, the tubercle bacilli had disappeared from the sputum, and the patient was able to return home, where the fillings were given by the family physician. In spite of two severe attacks of grippe, the patient has not lost a day's work, and has supported his family ever since. He is today well and stronger than ever before. He has kept up the fillings until the present time, but has now discontinued them.

CASE III.—A young, married woman, extremely frail, and almost unable to eat, who complained of an harassing cough, insomnia, and profuse expectoration loaded with tubercle bacilli. The patient had been ill for three years, and was unable to arrest the the process. The indications for the operation were: The profound cachexia, the failure of three year's symptomatic and tuberculin treatment, and the condition of the left lung, which was completely involved and riddled with destructive foci. In August the lung was compressed by Murphy's method without any difficulty, and by October the patient was riding, driving, picnicking, eating, and sleeping well. In December the patient returned home, the fillings were given, but an unwise mode of life converted what might have been a brilliant recovery into failure and death.

CASE IV.—Married woman, aged forty years, who had an harassing cough, and abundant expectoration loaded with tubercle bacilli. Eighteen months' rest in bed in the open air had failed to arrest the process or check the persistent hemorrhages. Over the entire right lung resonance and breath sounds were normal; over all the left lung there was dulness and the breath sounds were altered. At the level of the second left intercostal space, about 3 cm. from the sternum, there was a cavity. Indications for the operation were: Inability to check the process or the hemorrhages, and eighteen months of ineffectual efforts to recover.

In November, 1910, we cautiously began compressing the lung, fearing to burst the thin walls of the cavity. Using Murphy's method we succeeded without any difficulty, and in December of the same year the tubercle bacilli disappeared from the sputum. In May, 1911, the fillings were discontinued, and the lung allowed to expand. Today there is no cough, no sputum, and over the left apex there is dulness and irregular expansion, but over all the rest of the lung, normal resonance, and vesicular breath sounds are present.

CASE V.—Actor, aged twenty-six years, of frail, delicate physique. There were quantities of tubercle bacilli in his sputum. His history was that a few months previously there had been a violently acute onslaught of the disease, with high temperature, quick pulse, and repeated hemorrhages. This was a case of a deep, central lesion not well shown by physical signs. Normal resonance and breath sounds were present over the entire right lung. Over the left lung, to the fourth interspace in front and eighth rib behind, expansion was uneven, and there were numerous rales. The operation was indicated because of inability to keep down the temperature below 101° , or the pulse below 110, when the slightest physical efforts were made. After four months of inability to recover and the occurrence of a hemorrhage we concluded that the results of compressing the lung were more definite and certain in their effects than further waiting.

On November 1, 1910, the first filling was made according to Murphy's method. Since January, 1911, there has been no fever, no sputum, and the pulse has been 84. The tubercle bacilli have been persistently absent. Since April, 1911, no more fillings have been given, the lung has re-expanded, and resumed its function. Over all the lung there is now normal resonance and breath sounds.

CASE VI.—Woman, aged twenty-four years, frail and badly nourished, with an harassing cough, an abundance of tubercle bacilli in the sputum, and a temperature of 101° to 102° . For two years she had made ineffectual efforts in Colorado and elsewhere to recover. Over all the left lung there was dulness and there were somewhat suppressed uneven breath sounds and rales. The operation was indicated, since the future offered little more hope for

recovery than the past, and the harassing cough, anorexia, a rectal fistula, casts, and albumin were not encouraging.

In November, 1910, the first filling was made according to Murphy's method. Pleural adhesions, and the inability to endure enough pressure to break them up made the complete compression of the lung impossible. Nevertheless, the patient has of late only had fever during attacks of bronchitis in the right lung. Today she is in much better condition than a year ago. The breath sounds over the greater portion of the affected lung are suppressed, the casts and albumin have disappeared, and the patient is steadily improving. When this is contrasted with her former condition we have every reason to be gratified by the result.

CASE VII.—Actress, aged twenty-four years, fairly well nourished. The upper lobe of the left lung, and the upper and middle lobes of the right lung were involved. In the second intercostal space to the right loud, bronchial breathing and dropping rales were heard. Her temperature was 101° . She had a violent cough, profuse expectoration, and night sweats.

We hoped that the temperature was due to secondary infection of the cavity and that approximation of its walls would do more than anything else to benefit the patient. On November 1, 1910, the first filling was made. The results were most gratifying. The temperature fell to normal, appetite and strength improved. In April, 1911, the patient was able to ride and we began to hope that we could eventually allow the lung to reëxpand, and if necessary, compress the left lung. Unfortunately, the patient, tired of restraint, left the sanatorium.

CASE VIII.—Young, married woman. She was profoundly emaciated, had no appetite, and suffered from attacks of indigestion and high fever. The left lung was normal, but over the right lung there was absolute dulness down to the angle of the scapula, and complete suppression of breath sounds; above the angle there was harsh bronchial breathing; and over all the rest of the lung the breath sounds were suppressed and there were rales. This being an interstitial case, and trans-bronchial drainage failing us, treatment by compression seemed contraindicated; nevertheless, as recovery was otherwise impossible, we decided to make the attempt.

The first filling was made, according to Murphy's technique, without difficulty. On account of pleural adhesions it was impossible to compress the lung and pleural reflexes and pleural neoplasms made the attempts very difficult. After three months she had gained seven pounds in weight, was much stronger and better in every way. The temperature always rose after each filling, frequently as high as 104° , but there was no expectoration. The patient is better than a year ago, but we have given up the fillings, and do not expect a favorable result.

CASE IX.—Man, aged twenty-six years. He had been ill a year, with night sweats and severe diarrhea. Over the right lung dulness extended to the fourth rib in front, and the seventh rib behind, with altered breath sounds and rales. His temperature was 101° to 102° . The lung was compressed without difficulty, but the pressure had such a bad effect upon the gastro-intestinal conditions that it seemed useless to continue the attempts. The patient died in the winter of 1911.

CASE X.—Just after the attempt to compress the lung the patient had a severe hemorrhage, and died from aspiration pneumonia.

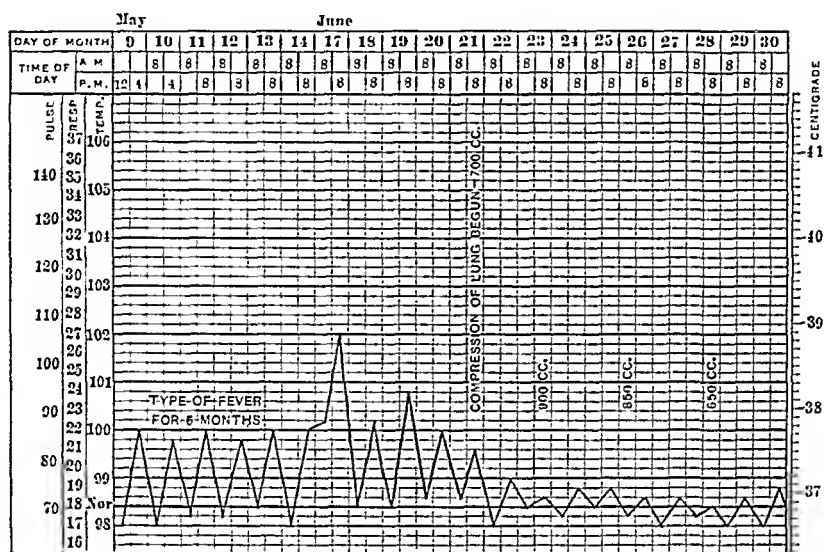


FIG. 4.—Chart showing favorable effect on temperature of compression of the lung.

Since June, 1911, we have had 14 cases, and while the results are too recent to be of any value, 6 of them are sufficiently interesting to report. Three of these cases showed a prompt and persistent fall in temperature to normal, save in 1 case during a short attack of bronchitis in the other lung. One of these cases had previously had skilled nursing for six months, with absolute rest in bed. His chart shows graphically the results of compression of the lung (see Fig. 4).

Another case was of the acute pneumonic type, with the bacilli in clumps so that it was impossible to distinguish the individual ones. There was rapid extension of the process for four months, with fever, inability to eat, and an exasperating cough. On May 27, 1911, the first filling was made. As soon as the lung began to be compressed the temperature fell to normal and has remained so

ever since. The tubercle bacilli are scattered singly through the field, the patient is feeling well, and keeping house.

In another case, rest in bed for weeks failed to reduce the temperature, but as soon as the lung was compressed the temperature became normal and has remained so.

A fourth case is that of a patient who for six months was unable to make any improvement in spite of complete rest in bed. In this case the temperature did not become normal until three months after beginning the compression of the lung.

In the fifth case the left lung was riddled with destructive foci. It was held fixed by extensive adhesions, and the pleural surfaces were covered with angiomatous vessels. Since compression of the lung was begun the breath sounds have been greatly suppressed; there are no rales, and the temperature is normal. There is a marked subjective improvement and gain in weight and strength.

The sixth case is that of complete involvement of the left lung. Instead of being a weak, bed-ridden patient, he is now feeling better than in years, and is independent in his actions. The lung is perfectly compressed, and there is no clinical suggestion of tuberculosis.

SUMMARY. There are hopeless cases of pulmonary tuberculosis which cannot recover with ordinary methods of treatment under the most favorable circumstances. There are also cases that are unable to hold a recovery after it has been made. In these cases, if the lung can be compressed, and kept so for a sufficient length of time, recovery will usually follow. Fifty per cent. of advanced cases treated by compression have been reported as permanently cured.

The durable nature of the recovery under this form of treatment is worth considering. Instead of the uncertain restraint of an encapsulating process, with all the dangerous factors of the disease merely rendered latent, we have their complete and permanent removal, and as a result the lung becomes healthy and clean. The disappearance of the tubercle bacilli removes a source of infection months before it can be accomplished in any other way.

The course of recovery is helpful subjectively. The certainty and precision of the method permit a great deal of liberty and the sense of security gives buoyancy to the patient.

When should we attempt to compress a tuberculous lung and when not? If complications exist, sufficient in themselves to forbid recovery, it will avail little to compress the lung. If the sounder lung is not too much involved, it may be greatly benefited by the removal of toxins from the other lung. At present it is generally agreed that only advanced and hopeless cases are suitable for the method. Forlanini, however, urges its use in early cases. Murphy says that the method is preëminently indicated in the early cases

because they forestall practically the only obstacle to success, namely, pleural adhesions.

A lung that is not densely infiltrated and has no adhesions is easily compressed, and the results are brilliant. The dangers and difficulties increase in direct proportion to the amount of lung infiltrated and held out by pleural adhesions, to the degree of obliteration of the pleural cavity, to the distention of the pleural vessels, and to the amount of clotting that has occurred in the pulmonary vessels.

A conservative plan is to give the patient every opportunity to recover by the usual methods provided always there is no danger in waiting. If, after persistent efforts, the temperature cannot be reduced, nor the extension of the process checked; if, after making a good recovery the patient is unable to hold it, but loses whenever any physical effort is made; or if there is some complicating factor, like vicious menstruation that predestines failure; then an attempt to aid the patient by compressing the lung seems amply justified.

LEUKEMIC TUMORS OF THE BREAST MISTAKEN FOR LYMPHOSARCOMA.

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THE case herewith reported is so remarkable that it deserves record. So far as we know it is unique, and from it one may learn several lessons. The history is as follows: A married woman, aged thirty-three years, was admitted to the hospital, June 13, 1911. She said that two weeks previously she had noticed a lump in the right breast which was not tender nor painful. It had not grown any since she noticed it. There was no loss of weight. She had one child, now aged eight years. She never had had any inflammation of the affected breast. Examination showed in the right mammary gland at its upper and outer quadrant a small nodule, the size of a hickory nut, not tender, nor cystic, firm to the feel, and not attached to the skin. No axillary nodes were palpable. The remainder of the breast contained no nodules nor were there any in the opposite breast.

On June 14, 1911, the tumor was excised. A frozen section at the operating table was not satisfactory so the wound was closed. A subsequent pathological examination showed the tumor to be

benign, the diagnosis being a lymphoma. The patient went home. She returned to the hospital five months later saying that after she had been home a month another small lump developed near the old scar in the right breast and this was followed by the appearance of two or three other lumps in the same breast. Two weeks prior to her second admission into the hospital, she noticed a lump in the left breast. All the tumors had been growing steadily larger since she first noticed them. She had had no pain in them and they were not tender. There was no discharge from the nipple nor was there any loss of flesh or strength.

In the right breast beneath the nipple were three hard, nodular masses, movable, circumscribed, not attached to the skin which was movable over the tumors. In the right axilla there was felt a mass the size of a hickory nut. In the left breast in its upper quadrant were two distinct masses, freely movable and hard. Nothing was felt in the left axilla. All the other organs were normal. The spleen was not felt. There were no other tumors anywhere, no enlargements of any of the lymphatics, except in the right axilla. The Wassermann reaction was negative. The patient was seen by Dr. Joseph A. Blake, who expressed the opinion that radical operations should be done on the breasts, since the tumors were probably malignant (sarcoma), although the outlook for a permanent cure was very gloomy. It was unfortunate that no blood examination was made at this time. Had a differential count been taken the true condition, leukemia, would have been evident and the patient spared unnecessary operations. She was examined by a number of men not one of whom suggested the advisability of a blood examination. To avoid such mistakes we would suggest in all institutions where it is possible, that a routine differential blood count be taken in all surgical cases.

On November 7, 1911, the radical removal of the right breast with both pectorals and the contents of the axilla was performed by one of us (McWilliams). Numerous enlarged glands were removed, one being from the very apex of the axilla. Perfect and undisturbed primary union followed this operation.

Pathological Examination. The nipple was not retracted but appeared normal. Throughout the breast substance particularly just above and outside the nipple were several rounded masses varying in size from a pea to a hen's egg. Between these larger masses could be seen, on closer inspection, small circumscribed lobules 3 to 4 mm. in diameter, in places closely packed together, in others arranged as strands and then sheets. These smaller masses corresponded in some instances to normal breast parenchyma, in others they were fringed about the large nodules. They differed from the ordinary glandular appearance of normal breast parenchyma in that they stood out from the stroma and showed their lobulated character very distinctly. The substance of the larger

and smaller nodules appeared the same. They were of a rather dull or grayish-pink color, firm and fleshy though not hard, quite even and homogeneous, showing no areas of necrosis nor hemorrhage nor trabeculae of any sort. The edges of the nodules were circumscribed, but showed no capsule and were seen to be attached to the surrounding subcutaneous tissues as an evenly outlined infiltration. The skin was nowhere attached to these nodules, but some of them were intimately connected with the fascia covering the muscle. There were many soft lymphatic nodes in the axilla varying from 0.5 cm. in diameter to 2.5 cm. They appeared evenly covered, dull pink, and homogeneous in substance. The muscles showed nothing abnormal.

Microscopic Examination. The nodules showed an enormous number of small cells with scarcely visible cytoplasm consisting chiefly of a nucleus, that is, round or ovoid, clear-staining, but containing particles of chromatin that often stained very deeply. These cells were supported by a delicate stroma clearly seen by Mallory's stain. There were few bloodvessels in the area, but where the cells were near vessels, the vessel wall was not disturbed. In less dense areas where in the gross small lobules could be made out, these cells were found to closely surround the acini and terminal ducts of the breast lobules and were chiefly confined to the intralobular stroma. No extensions into the muscle substance were found. At one point in the axillary tissues a vein was found containing a number of small, round cells which might have been lymphocytes or tumor cells from their appearance. The normal anatomy of the larger lymph nodes was somewhat lost. They showed no germinal centres and were made up of small, round, mononuclear cells resembling lymphoid cells. They showed chronic hyperplastic lymphadenitis. The diagnosis of lymphosarcoma was made.

With this apparently clear cut diagnosis, operation was performed on the left breast on November 15, 1911. The radical operation for removal of the breast with both pectorals and the axillary contents was performed. Considerable shock followed this second operation, and that evening the patient's condition was poor with a weak, irregular pulse, and considerable dyspnea. There was very little response to two saline intravenous infusions, so blood transfusion was performed at 9 P.M., her husband being used as donor without preliminary testing of the hemolytic action of the two bloods. Immediately before the transfusion the patient's red cells were 3,000,000, and immediately after it they numbered 4,000,000. Elsberg's cannula was used with good result. The next day the patient's condition was perfectly good, her pulse being strong and steady. There was likewise perfect and undisturbed primary union of the wound on this side. Pathological examination of the left breast showed conditions precisely similar

to those of the right breast with the exception that the nodules were considerably smaller and more isolated, while the lobular appearance of the breast tissue showed more distinctly.

One week later, at the suggestion of the pathologist, a differential blood count was made, whereupon the diagnosis was cleared up. It showed 117,000 white cells of which 90 per cent. were lymphocytes. The successive blood counts were as follows: November 22, leukocytes, 117,000; polymorphonuclears, 8.4 per cent.; lymphocytes, 90 per cent. November 27, leukocytes, 180,000; polymorphonuclears, 2.6 per cent.; lymphocytes, 96 per cent.; red blood cells, 3,000,000; hemoglobin, 65 per cent. December 2, leukocytes, 280,000; polymorphonuclears, 2.25 per cent.; lymphocytes, 96 per cent.; hemoglobin, 30 per cent. December 4, leukocytes, 250,000; polymorphonuclears, 1 per cent.; lymphocytes, 96.5 per cent.; red blood cells, 1,600,000; hemoglobin, 25 per cent.

On November 23 the patient began to have a temperature which became continuously higher each day until her death on December 14. On December 3 the examination of the eye grounds showed that in the left retina there were two hemorrhagic spots on the temporal half near the region of the macula. The right eye was normal. She was then transferred to the medical division, service of Dr. Janeway. On December 5, the edge of the spleen was felt for the first time on deep inspiration three-quarters of an inch below the costal margin and the gums of the lower jaw were swollen, spongy, tender and showed some small ulcerations, and the left tonsil was ulcerated. On December 7, she began to have persistent diarrhea, which continued until her death.

The report of the autopsy, performed by one of us (Hanes) at 7 P.M., on December 14, 1911, is as follows:

The subject is a small, emaciated female, measuring 160 cm. Rigor mortis not present. Both breasts have been removed by surgical operation, leaving normal scars. In the posterior triangle of the neck on both sides small, bean-sized glands are felt; the glands elsewhere are not enlarged. The mucous membranes are extremely pale. On incision the panniculus adiposus over the abdomen measures about 1 cm. The abdominal cavity is free from fluid and the peritoneum is everywhere glistening. The appendix is normal. All of the abdominal organs are free from adhesions, excepting the spleen, which is adherent to the lateral peritoneum over its lower third by old dense adhesions. Both lungs collapse upon opening the thorax and there is no fluid in either pleural cavity. The right lung is free from adhesions but over the posterior surface of the left lower lobe there are old adhesions. The pericardium contains about 50 c.c. of blood-stained fluid.

Heart. The heart is of normal size. Along the course of the anterior coronary artery there are hemorrhages under the pericardium, and along the lower half of the left coronary similar

hemorrhages are seen. The valves are normal and competent throughout the heart. The heart muscle shows no abnormality.

Lungs. Left: There are tags of old adhesions along the posterior surface of the left lower lobe, and for a space the size of a dollar on the diaphragmatic surface of the left lower lobe there are several small, yellow accumulations which can be torn from the underlying pleura and seem to be fibrinopurulent in character. The lung parenchyma seems normal on section. Right: The right lung is normal.

Trachea and Bronchi. The mucous membrane of the trachea and bronchi is very pale, otherwise normal.

Spleen. The spleen is enlarged, weighs 135 grams, measures 12 x 6.5 x 3.5 cm. It is adherent along its lower pole to the peritoneum, but can be separated from it without tearing the capsule. The spleen is moderately firm in consistence, the edge is rounded. On section the spleen maintains its shape. The splenic pulp is of a greyish red color, moderately firm, it scrapes off readily with the knife. The trabeculae are easily seen. Malpighian bodies are very indistinctly seen. There are small hemorrhages scattered through the substance of the spleen.

Liver. The liver weighs 1510 grams, measures 27 x 22 x 6 cm. The surface is smooth. The color is yellowish-red and finely mottled over its entire surface. These fine mottlings are from the size of a small pin-head to a match-head, and they do not project beyond the surface. On section the liver has about the appearance as seen through the capsule. The lobulations are not distinct. There are many small, whitish-yellow nodules scattered through the liver which range in size from a pin-head to a match-head, occasionally they are as large as a pea.

Gall-bladder. The gall-bladder and bile ducts are normal.

Esophagus. The esophagus is normal.

Stomach. The stomach shows no abnormality besides pallor of mucous membrane.

Intestines. The entire length of the small and large intestines is the seat of inflammatory changes in the mucosa which become more intense as one proceeds from the stomach. In the duodenum the mucous membrane is injected and red, and as one proceeds into the ileum this condition becomes more marked, and the mucous membrane is greatly thickened. Peyer's patches throughout the ileum are enlarged and in places slightly ulcerated. The lower ileum shows quite marked congestion and edema of its mucous membrane, and the crest of the folds are covered by a brownish, necrotic substance. The bloodvessels of the surface are markedly injected. As one passes the ileocecal valve, the congestion and edema of the mucosa is much more marked, and the crest of the folds of the mucous membrane shows a brownish, necrotic substance partially replacing the mucous membrane. The

same condition extends to the rectum where it is rather less marked than elsewhere in the large intestines.

Lymph Glands. The glands throughout the mesentery are enlarged from the size of a pea to a lima bean. Some are red and congested on section, while others show a pale yellow, succulent, homogeneous surface. The glands nowhere show necrosis. The retroperitoneal lymph glands from the diaphragm to the coccyx are enlarged. They form two parallel chains, each about 2 cm. in thickness. These chains are composed of glands which, on section, present a mottled yellowish-red surface in which no normal lymph gland structure can be seen.

The mediastinal lymph glands are not markedly enlarged. The bronchial glands, however, show moderate enlargement. At the bifurcation of the trachea there is a gland measuring 3 x 1.5 cm. On section part of the gland is anthracotic, but one gets the impression that this part represents the old gland while the remainder of the gland, which is pale-yellow in color, represents the hyperplastic glandular tissue.

Pancreas. The pancreas is extremely pale, its consistence is decidedly firm. On section the pancreas cuts with an elastic feel. The pancreatic duct is patent.

Tonsils. The tonsils are enlarged to the size of a hickory nut, and both, especially the left, show marked ulceration, its surface being covered with a brownish, necrotic mass. This necrosis has extended to the surface of the left anterior pillar of the fauces.

Larynx. The larynx is normal.

Thyroid. The thyroid is normal.

There are a few small glands along the course of the internal jugular vein which nowhere exceed the size of a small bean.

Genito-urinary Tract. Both kidneys are alike. They are of normal size. The capsule strips easily leaving a very pale surface. The stellate veins stand out prominently. On section the cortex stands out sharply from the medulla because of its pallor, which is marked. The cortex measures 6 mm., the striations are faintly seen. There are no nodular accumulations seen. Both ureters are moderately dilated but free from constrictions. The bladder is normal. The uterus and appendages are quite normal in appearance.

Bone Marrow from Femur. The marrow is not increased in amount, is soft and of a dark red color.

MICROSCOPIC NOTES. *Bone Marrow.* The normal structure of the bone marrow is well preserved, but its substance is occupied almost completely by one type of cell. This cell is a mononuclear with very scanty cytoplasm. The nucleus is vesicular, rather clear and measures on the average from 6 to 8 micra in diameter. An occasional megakaryocyte is seen and there are scattered through the bone marrow small islands of erythroblasts. There are a few

cells with plentiful cytoplasm and large, round, vesicular nuclei which look like myelocytes.

Lymph Glands. Throughout the body they present the same histological appearance, which will be illustrated by a description of a retroperitoneal lymph gland. The gross structure of the lymph gland is recognizable and the capsule is intact. Here, just as in the bone marrow, one type of cell largely predominates, namely, a mononuclear cell measuring on the average from 6 to 8 micra, the nucleus being vesicular and clear and the cytoplasm scanty. Small mononuclear cells with pyknotic nuclei are occasionally seen and there is an occasional normoblast.

Thymus contains a great deal of dense fibrous tissue, within the meshes of which are masses of mononuclear cells similar to those described in the lymph glands and bone marrow. No remains of thymic tissue are seen.

Spleen. The Malpighian bodies are present. They are composed of vesicular mononuclear cells similar to those described elsewhere. The splenic pulp contains a diminished quantity of red blood cells, its substance being largely composed of vesicular mononuclear cells with here and there typical mononuclear leukocytes. There are, in addition, large mononuclear cells with rather plentiful protoplasm, the nucleus being vesicular.

Liver. In the peripheral connective tissue there are occasional accumulations of vesicular mononuclear cells with an occasional normoblast and a few lymphocytes. There is a moderate grade of fatty infiltration of the parenchyma.

Kidney. In the kidney there is a patch of leukocytic infiltration, the cells here being of the same type as those described in the lymph glands and bone marrow.

Intestines. Both the small and large intestines show diphtheritic enteritis. The mucous membrane is desquamated over considerable areas. The bloodvessels of the submucosa are greatly dilated and there is a profuse inflammatory exudate which is composed almost entirely of lymphocytes, the prevailing lymphocyte being here a mononuclear similar to those described in the lymph glands and elsewhere. There are, in addition, many plasma cells.

A section of one of the breast nodules noted upon the second admission shows the following picture: There are alveolar structures lined by cuboidal epithelium with a distinct basement membrane, which are surrounded and embedded in a mass of mononuclear leukocytes. These leukocytes measure on the average from 6 to 8 micra, and the nucleus is round, clear, and vesicular. They are obviously the same type of lymphocyte as those previously described in the other organs.

To summarize, then, the case is surely one of lymphatic leukemia, with, however, very unusual features. The patient complained first of a tumor of the breast, and probably referred any slight

evidences of impaired health to this tumor, whereas the subsequent course of the disease and the autopsy show that the breast tumor was merely an incident in the leukemic process. The superficial lymph nodes were never enlarged. The spleen was not palpable until late in the course of the disease. A study of the various blood-forming tissues reveals a transformation from the normal to a tissue in which one type of mononuclear cell greatly predominates.

The patient developed toward the close a severe enteritis, and it is interesting that the type of cell which took part in the inflammatory exudate was the mononuclear cell seen elsewhere so abundantly, and not the polymorphonuclear leukocyte, a finding easily explained by the condition of the bone marrow, in which very few myelocytes were found.

OSTEITIS DEFORMANS, PAGET'S DISEASE, WITH REPORTS OF TWO CASES AND AUTOPSY IN ONE.¹

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THE occurrence of osteitis deformans is of sufficient rarity and clinical interest to make desirable the following report of a case which came under my care in the wards of the Philadelphia General Hospital. Incidentally it may be mentioned that one of the most complete and scientific studies of this disease was made upon a patient in that hospital and reported by Drs. Packard, Steel, and Kirkbride.²

Historical. Paget was not the first to describe cases of the disease, for he acknowledges the previous cases of Wilks, Rullier, and Wrany. Czerny had in 1873 described a case of spontaneous curvature of the long bones of the lower limbs, to which he gave this name. In 1876 Paget³ published an article which has given the disease a recognized place in our literature. In this paper he reported 5 cases that conformed to his classification. He subsequently reported two additional cases.⁴ It seems unfortunate that the affection should be called Paget's disease, because of the confusion resulting from this name being more generally associated with a peculiar form of cancer of the breast. It would seem more desirable to call it Paget's osteitis deformans, or, better still, to omit Paget's name.

¹ Read before the Section on General Medicine of the College of Physicians of Philadelphia, December 19, 1911.

² AMER. JOUR. MED. SCI., 1901.

⁴ Medico-Chirurgical Trans., 1882.

³ Trans. Path. Soc., London, 1877.

Butlin and Stegmann have reported a case showing the changes of osteitis deformans in the bones of prehistoric man. That the disease is not confined to man is evidenced in the report of its existence in the bones of lower animals.

Classification. The disease is to be differentiated from osteomalacia, rickets, leontiasis ossea, leuitic osteitis, osteogenesis imperfecta, tuberculous osteitis, achondroplasia, and general hyperostosis.

Many cases in the literature do not clearly belong to this category. The article by Packard, Steel, and Kirkbride reviewing all the reported cases up to 1901 eliminated all but 67 cases. Clopton,⁵ in 1906, states that the cases reported number 75.

Symptoms. Little of a definite character has been added to change Paget's description of the disease. "Most characteristic are the stooping posture, round shoulders, with head forward and chin raised as if to clear the sternum, loss of height, chest sunken toward the pelvis, pendulous abdomen, legs curved and held apart, knees slightly bent, the ankles overhung by the legs and the toes turned out. The enlarged cranium, square-looking or bossed, may add distinctiveness to these characters and they are completed in the slow, awkward gait and in the shallow costal breathing, which is compensated by the wide movements of the diaphragm and abdominal wall and the marked uplifting of the shoulders."

Subjective symptoms referable to the disease are vague and consist mostly of "rheumatic pains" in the parts affected. The insidious onset makes it difficult to determine the time of the first appearance of the disease. Paget states that it begins in middle life or later. Exceptions to this rule are evidenced in the cases of Sonneberg, of a girl, aged sixteen years; Maizard, a case, aged twenty-one years; and White, a man who had the disease when aged thirty-five years.

Parts Affected. The cranium and long bones of the lower extremities are the chief points of involvement. The lesions are usually symmetrical, but crossed involvement is often noted, *i. e.*, left leg and right arm. The left leg is most frequently first affected. The bones enlarge and soften. The location of the curvature seems to be determined by the superimposed weight, as is suggested by the spinal curvature with bowing and twisting of the femurs and bones of the legs. It has been pointed out that the deformity may be due to pathological increase in the length of the curved side of the bone. Neither of these explanations covers the cranial deformity, the patellar nodes, nor the exostoses on the arms and clavicles. The thorax frequently shows a resemblance to the rachitic type, the spine is curved and the vertebræ are fixed. The pelvis is broadened so that in the male it resembles the female type. The cranium is large, oval-shaped, with the broadest end up, and presents

inequalities in the surface. The arms seem disproportionately near the ground. The affected bones present localized nodes and circular thickenings. In some cases there were circumscribed painful swellings of the periosteum, which later subsided. The gait is "waddling." The two features of the disease that are most apt to attract the patient's attention are the increased size of the head in the male, noted because of the difficulty in procuring a hat to fit, and the loss of stature in the female, made evident by the necessity of shortening the skirts.

Etiology. Among the suggested causes are syphilis, cancer, arteriosclerosis, nerve lesions, including those of trophic origin, gout, and perversions of the secretions of the ductless glands. Syphilis of the hereditary type offers more probabilities of causation than does the acquired variety. Cancer is more often a terminal than an early condition. The evidence of any of the other suggested causes is inconclusive. It is safe to say that the cause of this disease is undetermined.

Heredity certainly exercises an influence. Chaufford⁶ reports the disease in mother and daughter; Berger,⁷ in mother and son; Smith,⁸ in father and son; Lunn, in two brothers; Pic, in two members of a family; Robinson, in two members of a family; Oettinger and Lafont, in father and two sons; Kilmer, in sister and brother. The sister of the case here reported shows the disease in a definite but incompletely developed stage.

Pathological Anatomy. The skull and long bones are most affected, but the spinal column, clavicles and patellæ are usually involved. Symmetrical parts are not always affected. The skull is greatly thickened, the sutures obliterated, and the Haversian canals effaced. The new bone is deposited on the outer table. There is no encroachment upon the capacity of the skull. In the early stages the calvarium may be cut with a knife or compressed between the fingers. It is very vascular and later undergoes defective ossification, characterized by deficiency of lime salts. The bones of the face are infrequently involved. The new bone is not deposited in the same way as in rickets. In osteitis deformans it is formed on the convex surface about the circumference of the bone, while in rickets it is placed upon the concave surface. The origin of this new bone, according to most writers, is periosteal. Von Recklinghausen, however, maintains that it is formed from the medulla. In the process of its formation there are successive stages of absorption and regeneration. Softness and bending of the bones are characteristic, but there are to be noted in various affected areas points of ivory-hardness. The uncalcified new bone being markedly elastic, the tendency to fracture, observed in certain other bone affections, is absent in this disease.

⁶ Osler's Modern Med., 1909.

⁷ Ibid.

⁸ Ibid.

Paget regards the disease as a chronic inflammation with: (a) rarefying osteitis, particularly of the compact bones, (b) formation of new bone from the periosteum.

Termination. Insanity has marked the late stages of certain cases. It has been pointed out that cancer is not as frequent as might be expected in persons as old as are most of these patients; nor is sarcoma as common as one would think likely in a disease which would apparently make a transition reasonable. The fatal termination seems to be in no way related to the bone changes.

Complications. Arteriosclerosis and cardiac disease are common. Emphysema, bronchitis, edema, pleuritis, cancer, Bright's disease, and insanity have been noted. Changes in the cord have been reported, but the findings have not been conclusive.

Diagnosis. It seems probable that few cases are overlooked and unrecorded. The greater frequency with which these cases are found in the recent literature would suggest a more general recognition of the disease. The earliest possible diagnosis may be made by the x -rays. The first report of x -ray findings in a case of this disease was made by Gallois in Gaillard's case. In it there was thickening of the diaphysis and calcification of the arteries of the extremity. The radius and ulna were also much thickened and slightly curved. The marrow was hypertrophied and its structure was altered. The ends of the joints were deformed, but the carpi were normal. In the head the shadows of the bone were darker than those of the neighboring bones. The humeri were thickened, but the elbow-joint was fairly intact despite the distinct alteration of the ends of the bones forming it. In Daser's case there was "thickening of the bones with irregular calcium deposits in the cortex," and encroachment upon the marrow cavity. In Hochkeimer's case the shadow of the marrow cavity had entirely disappeared. Schlisinger's case showed no involvement of the epiphysis. This speaks against the view that the disease is a modified form of arthritis deformans. Sonneberg found the bones of the pelvis to present an appearance similar to that of osteomalacia.

Differential Diagnosis. In mollities ossium there is not the same thickening of the bones as is seen in this disease, and the cranium is not involved. In fragilitis ossium the deformity is that which usually attends fractures. Acromegaly differs in the shape of the head and in the involvement of the lower jaw, superorbital arches, and hands. Leontiasis ossium effects chiefly the bones of the face. Hyperostosis canii is regarded by some as a stage of osteitis deformans, but others consider it a separate disease, since it does not involve the long bones.

Treatment is of no avail, and consists in palliation of the symptoms incident to the intercurrent diseases.

The following is a partial list of the cases reported since 1906, when M. B. Clopton summarized the previously reported cases.

There is a possibility that some of these cases have been included in his estimate of the number on record.

In 1906 each of the following reported a case: Bardenheur,⁹ C. Mackey,¹⁰ A. Saunders,¹¹ A. Tedeschi,¹² C. Sternberg,¹³ E. Modea and C. da Lana.¹⁴

In 1907 two cases were reported by Apert and Berwait,¹⁵ one each by H. Schlesinger,¹⁶ R. Waterhouse,¹⁷ and D. Stanley.¹⁸

In 1908 A. Herbert,¹⁹ Sinclair White,²⁰ B. Bramwell,²¹ J. H. Ramsburgh,²² K. Glaessner reported cases,²³ and J. Vergner²⁴ observed three.

In 1909 one case each was recorded by Klippel and Pierre Weil,²⁵ W. R. Hewitt,²⁶ Prescarlo and Bertoletti,²⁷ Bandy and Clermon,²⁸ H. Koch,²⁹ R. A. Hann,³⁰ F. Ravenna,³¹ two cases by R. Manwaring White,³² and three each by C. J. Bertlett³³ and C. von Kutscha.³⁴ Total 34 cases.

Report of Case. E. H., married, aged sixty-five years, admitted to the Philadelphia General Hospital August 15, 1910, complaining of shortness of breath, edema of legs, and a feeling of distress in the gastric area.

Family History. Mother died, aged ninety years, of apoplexy, father died, aged fifty-three years, of apoplexy; two brothers living, one has chronic indigestion, the other is healthy; three brothers are dead, one aged twenty-one years, of heart disease, the other two died in infancy; three sisters died in infancy; one sister is living, aged sixty-seven years, has renal and cardiac disease, and shows unmistakable evidences of osteitis deformans in the bones of the head and shortening of the legs without evident thickening of the long bones. She declines to submit to x-ray examination. The history states that the maternal grandfather died, aged ninety-eight years, the great grandmother, aged one-hundred and five years, and the great-aunt, aged one-hundred and eight years, the

⁹ Deutsch. med. Woch., 1906, xxxii, 525.

¹⁰ Lancet, 1906, i, 787.

¹¹ West London Med. Journal, 1906 xi, 27.

¹² Semano Med., Buenos Aries, 1906, xiii 993.

¹³ Verband. d. deutsch. path. Gesell., 1906, 137.

¹⁴ Margagni, Milan, 1906, xlviii, 337.

¹⁵ Bull. et mém. d. hôp. de Paris, 1907, xxiv, 235.

¹⁶ Mitt. d. Gesell. f. in. Med., 1907, vi, 67.

¹⁷ Lancet, May 4, 1907.

¹⁸ Lancet, 1907, i, 889.

¹⁹ So. Calif. Pract., 1908, xxiii, 400.

²⁰ British Med. Jour., 1908, ii, 1675

²¹ Trans. Medico-Chirurgical Soc., 1908, N. S., xxvii, 254.

²² Wash. Med. Annals, 1908, vii, 179.

²³ Mitt. d. Gesell. f. in. Med., Wien, 1908, vii, 98.

²⁴ Ann. d'ocul., Paris, 1908, cxi, 321.

²⁵ N. incong. de la Salpêtrière, 1909, Paris, xxii, 1 to 23.

²⁶ Interstate Med. Journal, 1909, xvi, 561.

²⁷ N. incong. de la Salpêtrière, Paris, 1909, xxii, 252 to 266. ²⁸ Toulouse méd., 1909, xi, 16.

²⁹ Verhand. d. deutsch. path. Gesell., 1909, 107 to 119.

³⁰ British Med. Jour., 1909, i, 135.

³¹ N. incong. de la Salpêtrière, 1909, 524.

³² Brit. Med. Jour., 1909, ii, 12.

³³ Yale Med. Jour., 1909, xvi, 367.

³⁴ Arch. f. klin. Chir. Bul., 1909, lxxxix, 758.

paternal grandmother, aged seventy-nine years, and an aunt, aged seventy-five years. There is no history of tuberculosis or malignancy.

Previous History. The patient was married at eighteen, and had one child one year later. There is no history of venereal disease or miscarriages. She had rubeola and parotitis in childhood, pneumonia at sixty-three. A tumor was removed from the left breast when she was aged twenty-three years, and it has not recurred.

Present Illness. About nine years ago she first complained of shooting pains in the legs, which sometimes would extend to the shoulders. Damp weather made them worse but they were not more severe at night. Three years later she first noted that her legs were curving and that the bones of the head were becoming "lumpy." She was unaware of any change in her spine. For three years she has complained of gastric symptoms and dyspnea, and lately of edema of the ankles.

Examination. Pale, poorly nourished, and about four feet nine inches in height, which is three inches shorter than she was eight years ago. Skin loose, cachectic appearance, muscles soft, flabby, and somewhat atrophied. In bed she persistently assumes an attitude with her legs bent under her, leaning on her elbows and her head bent forward. Forehead prominent and high, temporal and frontal bones thickened and parietal bone flattened. The head measures 65 cm. in circumference; from occiput to glabella superiorly, 39 cm.; transverse measurement between meatuses, 37 cm. Orbital cavities are overhung by the frontal bones. Beginning cataracts are the only abnormalities noted in the eyes. The chest is pigeon-breasted, the lower part of sternum depressed; the scar of the amputated breast is present; respiratory movements are shallow. Abdomen prominent and pendulous, walls are edematous, and a deep transverse furrow is noted near the free margin of the ribs. The liver is enlarged. The heart is displaced to the left, the apex beat is in the seventh interspace, the muscle tone is fairly good. There are signs of mitral regurgitation and aortic roughening. There is marked arteriosclerosis, and the pulse is of good volume and high tension. The lungs show edema at the right base. The spine shows a thoracic and lumbar scoliosis.

Arms: Biceps and triceps reflexes present on both arms, resistance to passive movement, and to movement against resistance is good in both arms, no abnormality in size and shape of bones. *Legs:* Marked edema extending to knees. External and anterior curvature of femurs and tibias, together with thickening and enlargement. Patient cannot bring knees together closer than 17 cm.³⁵ The ankles are overhung by the legs. Sensation is normal

³⁵ Circumference of each knee, 8 cm.; of pelvis, 92.5 cm.; intertrochanteric, 31 cm.; length of spine, 52 cm.; plantar arches normal.

in the arms and legs. Leg muscles are better preserved than are those of the arms. Knee-jerks normal. Babinski and ankle clonus absent. Resistance to passive movements good in both legs; movement against resistance is poor in both legs. Speech normal, memory poor, orientation and reasoning good. Station: Shoulders bent forward, arms hanging, head elevated. Gait: Slow, awkward, scissors gait with toes turned out.

Urine shows marked albumin, epithelial and granular casts, Bence-Jones albumin test negative. Weight 96 pounds, says it was 83 pounds five or six years ago. Blood: red blood corpuscles, 3,770,000; white, 6,200.

The autopsy was performed by Dr. A. G. Ellis, assistant pathologist to the hospital and his notes are as follows:

Clinical Diagnosis. Chronic interstitial nephritis; mitral regurgitation; chronic gastritis; osteitis deformans.

Pathological Diagnosis. Hypertrophy and dilatation of left ventricle; hypertrophy right ventricle; dilatation both auricles; chronic aortic and mitral endocarditis; fibroid myocarditis; atheroma of pulmonary artery; aorta and coronary arteries; emphysema and edema of lungs; bilateral hydrothorax; partial atelectasis of right lung; chronic nephritis (diffuse); chronic catarrhal gastritis and enteritis; red atrophy of liver; hyperostosis of bones of skull and of long bones.

Autopsy thirty-one and one-half hours after death. The body is that of a markedly deformed adult white female, 141 cm. (56.4 in) in length. Rigor mortis is present. There is pronounced edema of the lower extremities and hands and to a lesser extent of the chest and scalp. The head is enormously enlarged, the lower part of the face not sharing in this change and thus giving a triangular visage with the base uppermost. Measurements: Circumference of the head, 60 cm.; over the vertex from one ear to the other, 33 cm.; from the root of the nose to the external occipital protuberance, 40 cm.; bitemporal, 14 cm.; biparietal, 17 cm.; biaural, 15 cm.; angle to angle of jaw, 11 cm.; occipitofrontal, 40.5 cm.; occipitomenal, 20 cm.

Each side of the skull shows a prominence above the ear. These extend 5 cm. both anterior and posterior to the ear, and reach an elevation of 2 cm. They are practically symmetrical. Slightly above the site of the external occipital protuberance is a rounded elevation 6 cm. in diameter. The forehead is very prominent, this prominence reaching 7 cm. posterior to the supra-orbital ridge, where it rather abruptly terminates. The nose is decidedly broadened at the extremity, and the openings of the nostrils are large. The bones of the face are not appreciably increased in size.

The chest is narrow above and broadened below. The obliquity of the ribs is excessive, increasing from above downward. The upper ones are widely separated, the second and third being 3 cm.

apart at the junction with the cartilages. Circumference of the chest just above the nipple line is 73 cm.

The arms show relatively little change. The left humerus is moderately bowed forward, this being confined to the upper half of the bone. The right is slightly more bowed than the left, especially in the upper third. The forearms show no appreciable change except a slight outward bowing of the upper portion of the right radius and ulna. The hands appear normal.

The lower extremities are decidedly bowed outward. This change in both thighs and legs causes the internal condyles of the femora to be 18 cm. apart. The curving of the legs is practically equal on the two sides. The femurs are convex anteriorly and externally, the tibias the same, though in the latter the anterior bowing is more prominent. Circumference of left knee is 32.5 cm.; of right, 33.2 cm. From the left anterior superior iliac spine to the external condyle of the femur is 37.5 cm., between the same points on the right, 38.5 cm. From the internal condyle of the femur to the internal malleolus is 33.5 cm. on each side. The distance between the anterior superior spines is 26 cm. From the anterior superior iliac spine to the symphysis pubis is 15 cm. on each side. The feet show no noteworthy deformities, though the intense edema might mask some changes.

The superficial fat of the chest and abdominal wall is pale yellow in color; the muscles are pale, waterlogged, and flabby. The skin over the abdomen and lower part of the chest anteriorly is marked by numerous slightly elevated, firm, brownish patches, 2 mm. to 1 cm. in length. These appear to be sessile papillomas.

The peritoneum contains 300 c.c. of slightly blood-tinged fluid. The transverse colon is prolapsed, nearly to the level of the umbilicus. Liver is 5 cm. below the costal border. The diaphragm is at the level of the fourth rib on the right side, of the sixth interspace on the left.

The left pleura contains 350 c.c., the right 1000 c.c. of nearly clear serum. Thymus gland is not present. The pericardium contains 75 c.c. of clear serum.

The heart, especially the left side, is greatly enlarged. The right side contains clotted blood, the left is empty. The right auricle is dilated. The wall of right ventricle is firm and thickened, measuring 0.7 cm. The endocardium shows several firm grayish patches. The left auricle is dilated. The leaflets of the mitral valve are thickened and calcareous at the base. The tendinous cords are fibroid, and in most instances calcareous, the latter change extending into the papillary muscles. The endocardium of the left ventricle is gray at points. Some of the muscle columns are entirely fibroid. Those at the apex are stretched and flattened. Wall of left ventricle, 2.2. cm. thick. The muscle is pale red and very firm. The aortic leaflets are thickened and calcific at the bases. The aorta shows numerous yellowish patches, some of which are very slightly

calcified. The coronary arteries contain patches of thickening, but are not calcified. Weight of heart, 480 grams.

Microscopically the muscle fibers are granular and there is moderate increase of the interstitial tissue.

The left lung crepitates but slightly, especially near the margins, because of distended vesicles. It is grayish in color, externally and on section, and relatively bloodless. The posterior portion contains an excessive amount of serum. The right lung is similar except that the larger part of the upper lobe is collapsed as the result of pressure by the fluid in the pleural cavity. The branches of the pulmonary artery in both organs are extensively sclerotic. Weight of left lung, 280 grams, of the right, 335 grams.

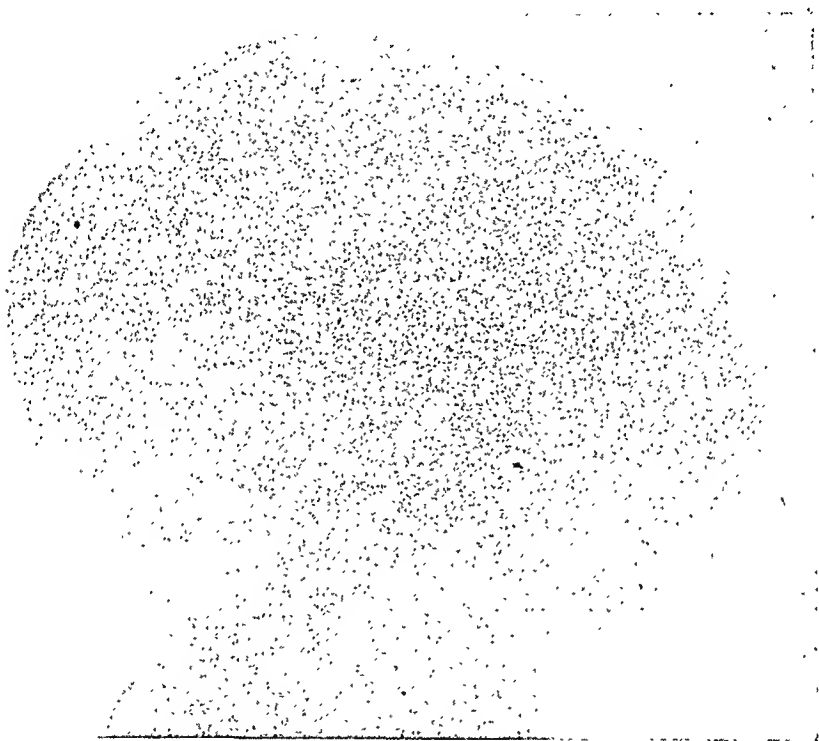


FIG. 1.—Large oval head in profile, showing enormous thickening of skull (1 inch) with porosity of the bones.

The thyroid gland is slightly more adherent than usual to the surrounding structures. It is pale red in color and very flabby. On palpation it is quite resistant, but is less firm on deep pressure than is the usual organ. Weight, 9.5 grams.

Microscopically the gland as a whole is deficient in colloid. Some areas contain the usual amount, an occasional acinus in these areas being dilated and overfilled. In the greater part of the organ the acini contain only a very small colloid content or, in the majority, are devoid of that substance. The latter acini show desquamation of the lining epithelial cells which are scattered

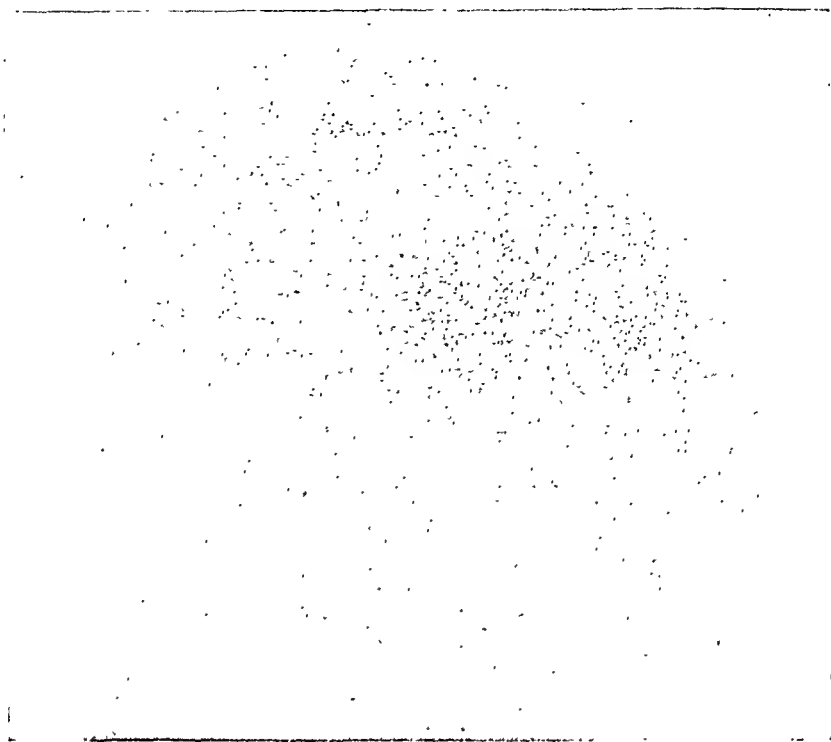


FIG. 2.—Another view of head in profile, showing marked thickening of bone and increased porosity.

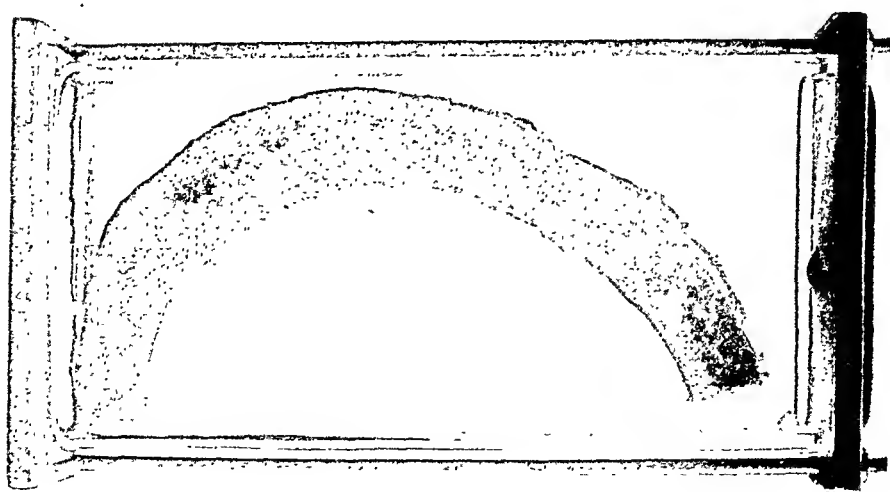


FIG. 3.—Section of skull, showing thickening of the bone (one inch), marked irregularity of the convex surface, defective ossification, and uneven distribution of compact tissue.



FIG. 4.—Bones of forearm, curved above and rarefied at lower ends.

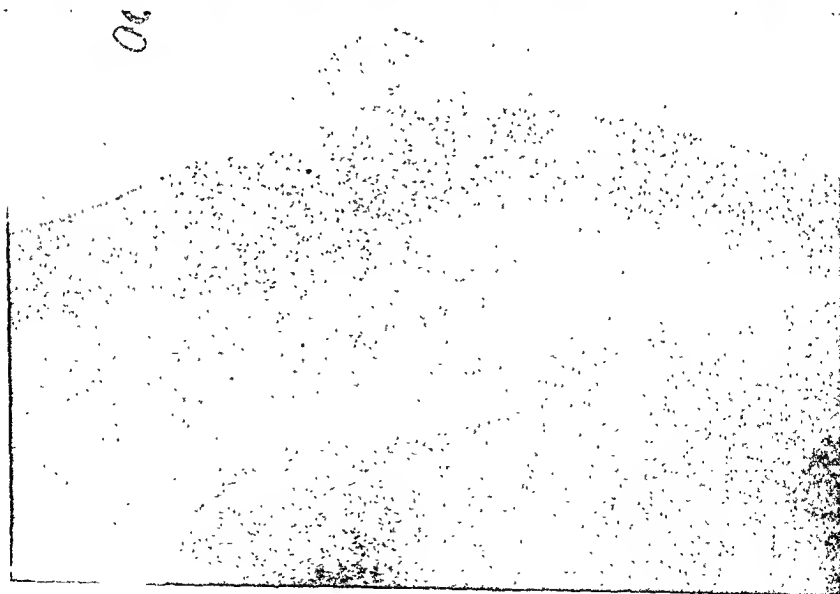


FIG. 5.—Femur showing curvature, thickening of the compact tissue and encroachment upon the medullary cavity.

promiscuously through the lumina. These cells also show decided changes in the cytoplasm, consisting of granular degeneration or even disintegration, many of the cells being little more than nucleus with possibly a few adherent granules of cytoplasm. In the acini partly filled by colloid the epithelium shows almost as great a change as that just described. In most of those containing the usual amount of colloid the lining cells are still adherent to the walls, and show less prominent cytoplasmic change, although at least

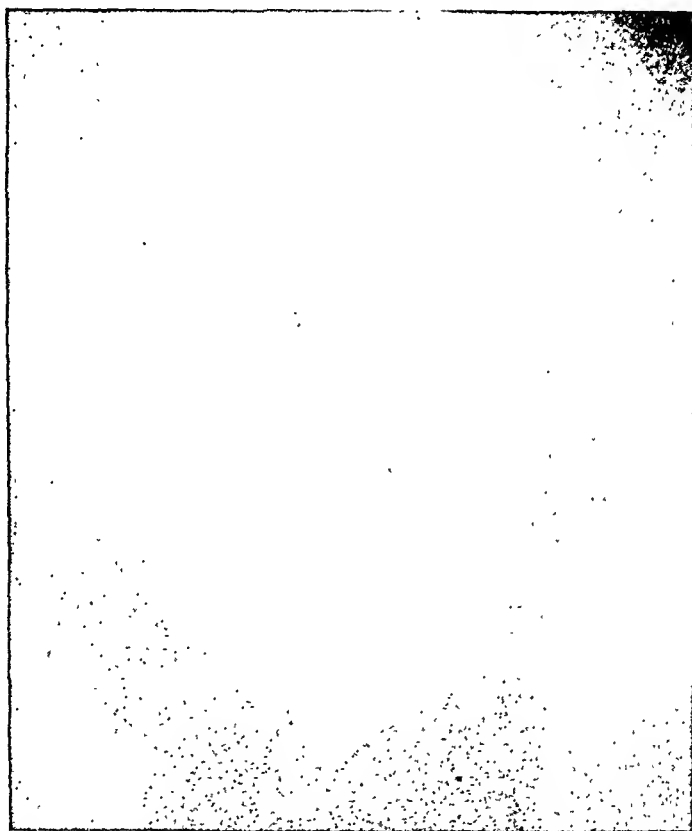


FIG. 6.—Marked outward curving of tibia and fibula with great thickening of the compact structure of shaft and irregular encroachment upon medullary cavity.

granular degeneration is present. The interstitial tissue of the gland shows no pronounced changes. Occasionally there are small circumscribed collections of mononuclear cells which encroach upon the neighboring acini. The small bloodvessels are decidedly engorged. Bodies supposed at autopsy to be parathyroid glands prove on section to be small masses of thyroid tissue.

The spleen is small, very firm, and the pulp is dark red in color. Weight, 115 grams.

The left adrenal shows no noteworthy changes. Weight, 5.5 grams.

The left kidney has a moderately adherent capsule. The underlying surface is granular. On section the organ is grey and the cortex is in many areas narrowed. The pyramids are dark bluish in color. Weight, 125 grams.

Microscopically the epithelium is granular and disintegrating, and there is considerable increase of connective tissue.

The right adrenal appears normal. Weight, 5.2 grams.

The right kidney is same as the left. Weight, 115 grams.

The ureters and bladder show no gross lesion.

The uterus contains an interstitial fibromyoma 1 cm. in diameter; otherwise it is normal. The ovaries are masses of fibrous tissue containing a few small cysts.

The gastric mucosa shows numerous dark red areas, largely postmortem in origin. The mucous membrane is not appreciably thickened.

The liver has a linear depression running the entire length of the organ, parallel to and 5 cm. above the lower border. This furrow is 2 cm. wide and 1 cm. deep. The capsule is thickened here and incision shows the fibrosis confined to that structure. The cut surface of the liver is dark red, and shows slight mottling. The organ is rich in blood. Weight, 1360 grams.

Microscopically there is an excess of blood in the central veins and adjoining cells are atrophied. The cells show granular degeneration.

The pancreas presents no noteworthy changes.

The intestines are normal. The thoracic and abdominal aorta contains many yellow patches in the intima.

The scalp over the lateral prominences already described is 2 mm. thick. Over the midportion of the skull it is 0.8 cm., but here it is very edematous. It is nowhere markedly thinned. Exposure of the skull shows on each side of the median line, posterior to the ear and extending nearly to the occipital protuberance, a dark-red area apparently due to blood beneath the pericranium. The bone saws with great ease. The skull in the median line at the anterior margin of the saw cut is 2.5 cm. thick. Posteriorly it is 1.7 cm. and at the lateral angles of the cut, 1.5 cm. thick. The external table has practically disappeared as such, the bone being spongy or at points decidedly porous. For the most part this extends the entire thickness of the skull, but at points there is relatively dense bone corresponding to the internal table; this is especially true of the lower lateral portions where a diploic zone is hardly distinguishable. The upper lateral portions and the vertex show a distinct diploic zone up to 1 cm. or slightly more in width. Of the remaining denser, but still relatively soft, bone about two-thirds is internal, corresponding to the internal table,

one-third external corresponding to the external table. In these areas the diploic tissue is very porous and vascular, and can be readily indented by the fingernail. At a few points in this zone are small islets of dense white bone, a few attaining 1 cm. in diameter.

Sections including the entire thickness of the bone were made from the lateral portion where the skull is practically uniform, diploic structure being unrecognizable. The thickness here is 2 cm. The microscopic structure is almost uniform the entire length of the sections, the extreme dural portion being only slightly more dense. In general it may be described as fibro-osteoid tissue. In all except some portions of the inner extremity the fibrous tissue slightly exceeds the osteoid in area. The latter contains no normal Haversian canals, and shows no normal lamellation, lamellæ, except in occasional areas, being entirely absent. What correspond to bone cells are numerous, but they appear immature and are in ill defined spaces.

The fibrous tissue occupies the greatly enlarged Haversian canals, and is mostly loose and cellular; in limited areas it is in the form of closely placed fibrils forming denser masses which stain deeply by Van Gieson. This tissue is everywhere very vascular. For the most part there is a sharp line of demarcation between it and the osteoid tissue, but at points where the former is densest the two gradually merge, giving the appearance of the osteoid tissue being transformed into the fibrous. The osteoid tissue is a little more prominent in what corresponds to the inner table. Sections from some blocks contain near the midpoint some quite large spaces in a matrix of mono- and polynuclear cells, marking the site of the diploe, but these areas are small.

In some sections multinuclear giant cells are quite numerous in the connective tissue, most of them being in contact with, or even nested in depressions in the osteoid tissue, resorption of the latter being in such instances very apparent. A few corpora amylacea are in the fibrous tissue. Both the pericranium and dura mater contain small islands of osteoid tissue.

The brain is pale in color, especially at the base. It is fairly firm, and shows no definite lesion. The basal vessels show only tiny scattered patches of sclerosis. Weight, 1.025 grams. The spinal cord shows no gross lesion.

Microscopically neither brain nor cord shows any noteworthy departure from the normal.

The hypophysis has a flattened anterior lobe, from above downward. The posterior lobe is very soft and was damaged in removal. The organ is not enlarged. Weight, 0.57 gram.

Microscopically the gland in general does not stain well, but there is no decided change in the anterior lobe except that all the cells are granular. Eosinophile cells are fairly numerous, but the

granules are not deeply stained. Masses of colloid in the acini are numerous. Only a fragment of the posterior lobe is attached.

Summary of the features of the case here reported: Woman of advanced years, indefinite history of onset, rheumatic pains, admitted to the hospital for symptoms in no wise related to the disease, deformity of the head, loss of stature, and swelling of the legs had been noted by the patient. These were confirmed on examination, and the bony increase detected as well as the spinal curvature. The x-rays and autopsy corroborated the findings.

A sister of the patient has the same disease in an early stage.

I desire to thank Dr. Walter J. Daly, resident physician, for his assistance in the preparation of the notes of the case, and Dr. Philip F. Williams for the study and report of the cultures; also Dr. Leonard Frescoln for the x-ray studies.

NOTE ON THE VALUE OF NITRIC ACID IN CAUTERIZING WOUNDS MADE BY RABID ANIMALS.

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THE application of nitric acid to wounds made by the bites of rabid animals is something more than a conventional method of medical treatment. It offers a rational interpretation of many things in the prevention of hydrophobia that are usually ascribed to the diffuseness and loitering motion of the "virus," to that errant motion which sometimes occasions it to lose its effect or its paths of connection with the central nervous system. This paper, which is deductive in aim, is chiefly concerned with the finding of arguments that support the simple proposition that cauterization with nitric acid is in itself an immediate source of safety. The idea is to ascertain how far, by fitting a homely remedy to people in a state of probable infection, that sort of security and that quantity of security may be imparted which the physician rationally may hope to impart.

The agencies requisite for the production of the kind of security just mentioned are: (1) Hemorrhage, by which is meant the momentary and unrestrained bleeding after the bite, and (2) cauterization, that is, the destruction of the "virus" and the parts in close connection with the outlines of the wound. The more powerful and diffusible the caustic the wider will be the range of its powers, both

for purposes of destroying first and cleaning afterwards. The distinction between valid cauterization and methods less technically competent, between caustics in the strict sense and antiseptics, with which they are often confounded, will be strongly marked in the character of the caustic employed. If nitric acid be used, instead of one of the numerous antiseptics in favor, the process will resemble actual burning, with the addition of washing.

It is the mistake of much popular medicine to suppose that wounds do not heal after nitric acid. Experience at the Department of Health of New York City does not support this view. Care must be taken, however, to clean the skin, and not to apply the acid too extensively to the bloodless, bony, or cartilaginous parts of the body. It is a good practice to draw up a small quantity in a capillary pipette, and deposit it drop by drop in the wound. This avoids risk, realizes the greatest amount of effect, and facilitates measurement. It enables the physician also, from time to time, to see what progress he makes and how far he avoids any needless pain or uninfected tissue. If the wound be uncommonly severe, or the case is that of a child, chloroform anesthesia is required, a precaution that should always be borne in mind. Such is the technique of this method of cauterization which, in spite of its simplicity and excellent effect, is strangely undervalued by the profession generally, as well as by those who have some favorite hypothesis to maintain. An instance is supplied by some remarks of Remlinger,¹ still more explicitly developed by A. Marie.² According to the first of these writers, cauterization is ineffectual if performed an half-hour after a bite. "It cannot be affirmed too strongly," says Dr. Marie, "that no cauterization can protect from hydrophobia." If this were a true representation of the scheme of cauterization, we cannot wonder that some doctors should consider it an unnecessary attendant on vaccination against rabies. To many others the remark may well seem needlessly skeptical and greatly overdrawn.

There has been a notable increase lately in wounds made by the bites of animals. At the Department of Health we see many cases peculiarly ill-treated and neglected. Many of these come from places outside the city, but New York itself (with the advantage of newspaper mouthpieces) offers many an instance in point. It is not easy to form an accurate estimate of the mischief done; it must, however, be wholly disproportionate to the pain or trouble inflicted by the use of nitric acid. Although pain may be allayed in a great measure by the application of anodynes, since errors in the treatment of bites have a many-sided interest, it is clearly worth while to undertake a systematic defense of the true method.

¹ *Bacteriotherapie, Vaccination, Serotherapie*, 1909, p. 81.

² Kraus and Levaditi's *Technik und Methodik der Immunitätsforschung*, Ergänzungsband I.

The incurable optimism of doctors is responsible for two deplorable events: (1) Now that they have come to rely almost exclusively upon vaccination in suspected rabies, many have ceased to pay sufficient attention to cauterization; (2) a multitude of remedies (and theories) have acted in competition with a combined force to blunt the critical powers of the mind.

The invaluable agents of cauterization, nitric acid, the much weaker silver nitrate, and actual burning (with which the mind readily associates excision) have been driven into neglect by dubious novelties and the increasing accumulation of rival eccentricities in medicine. The controversy as to the merits or the demerits of caustics is worldwide; but it is not, as I regard the case, a controversy on Pasteur vaccination, but on an auxiliary treatment, and in especial on the methods of that treatment. Strictly speaking, cauterization is not a treatment of hydrophobia at all, but a mechanical agent for destroying the poison, subsidiary to the main agent, the specific vaccine.

The principal object then proposed in this paper is to reaffirm in all its rigor and in a pointed manner, the rule that the application of *fuming* nitric acid is the most effectual means of destroying the "virus" of rabies in wounds, and that in all cases in which we fear its coexistence with a bite, it should be got rid of as far and as quickly as may be possible; and further, and above all, to choose from literature and common experience incidents and examples that violate or observe this rule. The principle has already been expressed in plain, emphatic language, in this country by Cabot;³ in England by Gowers;⁴ in Europe by Babes and Lentz.⁵ The subject is indeed important. To destroy the "virus" before it has germinated in the wound is the means sometimes of wholly avoiding the disease which it provokes. No more need be said of the technique, which is simple and direct, and entirely adapted to a particularly prompt mode of application. But, it has the high merit of paving the way for the subsequent success of the Pasteur treatment. These are facts determined in more researches than those I have quoted, and in some hitherto unpublished ones by Poor,⁶ which I shall quote directly.

It has therefore appeared to me that the endeavor to produce or enlarge this capability of treatment is one of the best services in which a physician can be engaged; and this service, excellent at all times, is especially so at the present day. The reasons of this belief I have already touched upon, but they may be extended as follows: (1) Hospitals, which are apt to prefer the pursuit of some safe and neutral method, furnish almost incredible instances of

³ Med. News, March 18, 1899.

⁴ Manual of Diseases of the Nervous System, ii, 940.

⁵ Vorträge u. prakt. Therapie, 1910, 3 s., Heft 10, 762.

⁶ Made at the Research Laboratory, Health Department, New York.

bites treated according to convention, the fruitful parent of error; (2) the practitioner in private may be careless from the belief that the case is one for expert rather than ordinary treatment; (3) chemists, apothecaries, and even the newspapers, called by an instinct that gets the better of everything else, exercise not only their own but all other crafts with extraordinary diligence, and accordingly treat bites with those two self-sufficient things—ignorance and irresponsible advice; (4) men who pose as clever in the science of drugs are dissatisfied with caustics, or at least but partially satisfied, hoping to find the ideal form. Much current medicine of a colorless, aimless kind is the work of these purists, whose opinions are wholly influenced by authority. Is this negative method ever likely to command old truths or bring to light new ones?

It is, of course, strict convention to sew up a bite. But this generalized method of treatment has not the happiest results. A striking fraction of deaths from hydrophobia is made up of those whose wounds have been closed with stitches. Viala⁷ cites many cases from the Pasteur Institute. How significant is his phrase, "*la plaie est fermée par 8 (or 6, 3, or 2, as the case may be) points de suture, et n'a pas été cautérisée?*" It recurs so often in the histories of those who have died from hydrophobia. From such constant uniformity valuable lessons may be drawn. Wounds made by rabid animals should not be sewed up; they should be allowed to bleed. Medically, or scientifically, the point is very serious. The retention of the "virus" destroys the whole balance of safety. For it is a fundamental thing about this disease that a nervous system once infected is not restored by Pasteur treatment. Hence, the use of stitches, instead of caustics, washing and dressing, is a gross and gratuitous blunder; stitches being the means of fructifying the "virus" and very little to the purpose in wounds of this character. It is the destruction of the poison that counts, not the mere healing of a "solution of continuity." The distinction is sound; yet it is overlooked in many hospitals.

In this matter as in all others we have become specialists; the bites of animals cannot be treated as ordinary wounds, even by the most fastidious surgeon, working exquisitely. They do not, it is obvious, require the utmost address; but neither are they to be dealt with according to the accidental tendencies of "schools," "methods," and the like. But worse than any treatment founded on misconception is treatment founded on the notion that any cauterization whatever is of itself useless.

It is a custom that seems a remnant of early medicine to cauterize with carbolic acid. Fermi, among moderns, seems to like it, but Babes⁸ has more than once shown its inadequate power.

⁷ Annales de l'Institut Pasteur, 1909, p. 512; 1908, p. 558; 1907, p. 486; 1906, p. 511, etc.

⁸ Connaissances médicales, May, 1887.

"*Ce virus est peu sensible à l'action de l'acide phénique*," he wrote long ago, and subsequent experience is confirmatory of this assertion.⁹ Sawtschenko,¹⁰ writing in 1911, says: "A solution of phenol, 0.5 per 100, failed to destroy fixed virus, even in twenty days." Fermi,¹¹ writing a few months later than Sawtschenko, seems aware of the relative weakness of carbolic acid. Of local methods, he adds, the hyperemia of Bier is the most effectual. He applied it, however, only in experiments on mice or rats. Nevertheless, carbolic acid is widely employed as a caustic. I find several instances quoted in the pages of Viala,¹² but only the blank fact that these cases were cauterized with carbolic acid, and that they died of hydrophobia is conceded to us.

The definition, or rule, of treatment, that we are seeking is to be found in the characteristic attributes of nitric acid, namely, its fluidity and caustic power; and the earliest paper that experimentally helps us to determine these attributes is that lucid one by Babes and Talasescu.¹³ It is here shown that the Paquelin cautery and the strong mineral acids are of equal power in protecting animals from rabies. This is also the conclusion of Marie,¹⁴ though arrived at in a different way. There are later experiments which show that with cauterization with nitric acid animals may be rendered in many instances secure from rabies. In Poor's experiments, to which I have already referred, 41 per cent. of his animals were saved, while all his controls died. Cabot's figures, derived from experiments with nitric acid, are even higher, but they are less searching, less convincing. Of profound interest is the fact, as all these experiments show, that cauterization is of value as late as twenty-four hours after inoculation. Hence it is that Ravenel¹⁵ writes: "There is strong experimental evidence that the free use of nitric acid will save a certain proportion of cases even after a lapse of twenty-four hours;" and Stimson that: "The best method is to thoroughly touch the wound down to its depth with nitric acid."

Next in importance comes mercuric chloride. Would not washing with a solution of this substance suffice? This is the belief of Hogyes who thinks caustics "illusory." A sense of false modesty shall not prevent us from thinking our own doctrine the better. When we have produced free bleeding, cauterized with nitric acid, and dressed with bichloride, we have done, humanely speaking, the right thing.

Yet so strange are the obliquities of disease, and in particular, of hydrophobia, that those whose minds are much influenced by this fatality will often be tempted to think that there are no fixed

⁹ *Centralbl. f. Bakteriöl.*, Band iv, 1910, S. 27; *Bulletin de l'Institut Pasteur*, 1910, p. 677.

¹⁰ *Annales de l'Institut Pasteur*, 1911, p. 495.

¹¹ *Archivio di Farmacologia sper.*, 1911, vol. xi, Fasc. iii-iv, p. 152.

¹² *Annales de l'Institut Pasteur*, 1910, p. 678.

¹³ *Comptes rendus de la société de biologie*, 1907, Tome ii, p. 430.

¹⁴ *Hyg. Lab. Bulletin*, 1910, p. 52.

¹⁵ *Ibid.*, 1894, p. 435.

principles for its therapeutics to rest on. It is perhaps this spirit which allows the disastrous use of palliatives, iodine, alcohol, and, as one writer recommends,¹⁶ common vinegar.

It is a fact that cauterization of any kind, that is, the application of anything that has the essential quality of caustics, is a valuable means of saving life. According to the writer in Eulenburg's *Real-Encyclopädie*, many are saved in this way in Germany; according to Hogen cauterization has increased the percentage of cures from 19 to 41 per cent.; according to Proust,¹⁷ "Of 117 people bitten but not cauterized 76 died; while of 249 cauterized only 89 died," all of which shows the high empirical probability of the value of cauterization.

Statistics, it is obvious, do not finally solve problems. Instances gathered in this way make simple calculations of probability not causal connections. It is a method auxiliary to scientific induction so-called, and a causal connection between cauterization and a certain uniformity of result may be inferred by comparing the averages of cases in animals with the average of especially enumerated cases in humans, which are conditioned by the same factor. This process leads us to the possibility of establishing strict uniformity among cases cauterized and cases protected from hydrophobia.

THE MEDICAL ASPECT OF CHRONIC TYPHOID INFECTION (TYPHOID BACILLUS CARRIERS).¹

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It has proved interesting and instructive in connection with the subject of this paper to review the opinions held by teachers of medicine twenty-five years ago relative to certain infectious diseases. Until about two decades ago studies in the problems of immunity were hardly begun, while the science of bacteriology was in its infancy. In fact, because of the rapid development of the science rather than the art of medicine, it may be safely asserted that more progress has been made in our understanding of the early and late effects of infectious diseases during this period than had been possible during the centuries preceding. This progress has been made possible through the labors of the early investigators, and it is more fortunate for the coming generations than we can

¹⁶ Töpfer, *Klin. Jahrb.*, 1907.

¹⁷ *Annales de l'Institut Pasteur*, 1894, 435.

¹ Read before the Mississippi Valley Medical Association at Nashville, Tennessee, October 17, 1911.

conceive that there existed such creative minds as those of Koch, Pasteur, Virchow, Ehrlich, and Wright.

We now understand, tentatively at least, many facts not available even a decade ago regarding the late effects of certain infections. The early effects were more readily recognized clinically, while less importance was attached to the remote sequelæ except in so far as certain complications retarded individual recoveries. Little was thought then of the late effects of certain infections upon the mass-hygiene or sanitary condition of communities. For example, one decade ago but little importance was attached to the bacteriological condition of the child's throat subsequent to diphtheria, and the importance of the subject was not appreciated. It was hardly considered possible that many such children became chronic carriers of the infection for weeks or months subsequent to their attack. We now realize that a large percentage of the disease incidence arises in others from exposure to the mouth and throat secretions of such individuals. Nor in tuberculosis was it generally recognized that many individuals with chronic non-active types of the disease served as disseminators of the infection for periods of years, while themselves able to enjoy the blessings of apparent health.

Likewise, in typhoid fever, an ever present disease in our American municipalities, and in Asiatic cholera, the remote effects of these infections have only recently been appreciated. It is now generally recognized that about 4 per cent. of all typhoid cases become chronic carriers and disseminators of the infection for periods of months or years after their apparent recovery. It is entirely possible for the human body to harbor disease microorganisms of many other types for long periods of time without interfering with the apparent health of the individual. Sternberg discovered the micrococcus of pneumonia in healthy sputum, and every physician is familiar with the latent forms of syphilis and tuberculosis, which for long periods remain quiescent, and do not lead to destructive tissue changes. The various factors of immunity which protect the individual in such instances are not understood, but are generally covered by the explanation, so frequently given, but which serves merely to cloak our ignorance, the resistance of the individual and the varying virulence of different strains of bacteria.

In considering typhoid fever we have to deal with the following two modes of dissemination:

1. The spread of the disease by means of water, milk, and food products contaminated directly or indirectly by some active typhoid infection, but, as a rule, *remote* from the source of infection.

2. By contamination of water, milk, or food products *directly*; that is to say, by typhoid bacillus carriers who are in some way connected with the handling of food supplies.

We recognize two types of chronic typhoid carriers—"contact,

idiopathic or primary carriers," who have never had the disease to their knowledge, and "secondary carriers," who have at some time previously had the disease.

PRIMARY, IDIOPATHIC, OR CONTACT CARRIERS. Typhoid carriers who become such through association with the disease, and such instances are not uncommon among nurses and orderlies, but who themselves have not had typhoid to their knowledge, are called "contact carriers." Since every typhoid patient requires the constant care of at least two or three individuals, it may readily be surmised that a large percentage of such attendants become "contact carriers." In many instances such individuals continue to excrete typhoid bacilli in the stools and urine for periods of years. Their own tolerance to the infection is probably due either to natural immunity or to a partial immunity from an earlier unrecognized mild typhoid infection.

Houston,² in 1899, reported the first case of persistent typhoid bacilluria in a contact carrier, who for three years had shown symptoms of chronic cystitis, while Drigalski and Conradi,³ in 1902, found typhoid bacilli in the stools of 4 persons who had had no previous typhoid fever symptoms, but who had been in contact with typhoid fever. Park⁴ has estimated "that probably one in every 500 adults who has never knowingly had typhoid fever is a typhoid-bacillus carrier." At first glance such figures are appalling, but with our recent knowledge of so-called "short duration typhoid" and of other factors, such as individual resistance and the varying virulence of different strains of bacteria, we can appreciate how many individuals at some time during their lives suffer an active typhoid without themselves being aware of it. In fact, it is entirely possible that many so-called summer diarrheas are in reality mild typhoid infections, which are not so diagnosticated. Such individuals receive a partial immunity, partial in the sense that, while themselves protected against the damaging influence of the infection and experiencing little subsequent disturbance, they are able to harbor, excrete, and perpetuate the bacilli in large numbers. Bacilli from such individuals when engrafted upon non-immune soil are able to produce all the clinical evidences of a severe attack.

SECONDARY CARRIERS. As above mentioned about 4 per cent. of all individuals who have, to their knowledge, had typhoid become chronic carriers of the disease for periods of months or years. They have secured from the previous attack only a partial immunity in the sense that while certain protective immune bodies, such as the opsonins and stimulins, are augmented by the attack, others, such as the bactericidins and bacteriolysins, for some

² Brit. Med. Jour., January 14, 1899. *ibid*, October 9, 1909.

³ Quoted by Park, Jour. Amer. Med. Assoc., September 19, 1908.

⁴ Jour. Amer. Med. Assoc., September 19, 1908, p. 981.

unknown reason, are not augmented to the point of destruction of the bacilli. In other words, the factors which protect them individually from further damage do not lead to complete destruction of the infection, that is, their immunity is phagocytic, not bactericidal or bacteriolytic. Experience has shown that many typhoid bacillus carriers experience comparatively little discomfort. The attention of the physician is secured either because of their probable connection with endemic outbreaks or from individual symptoms, vague in character which lead to an investigation.

Fütterer⁵ in 1888 first called attention to the presence of typhoid bacilli in the gall-bladder, while Gilbert and Giroche, in 1890, are generally credited with the first description of typhoid bacillus cholecystitis. In 1893 Chiari⁶ was able to collect 13 instances of typhoid bacillus cholecystitis and, in 1898, Cushing⁷ tabulated 6 cases. The articles by these investigators and the paper by Ehret and Stolz⁸ in 1900, in which 32 cases were described, had much to do with the recognition of the importance of the subject. Much discussion has arisen concerning the way in which typhoid bacilli reach the gall-bladder. The recent work of Chiari,⁹ Hirsch,¹⁰ and Forster¹¹ and of Foster and Kazsen, would seem to convince most of us that the infection reaches the gall-bladder, in most instances, from the liver secretions or by way of the blood stream. Such mode of transmission undoubtedly occurs in contact carriers who have had a typhoid bacteriemia without the clinical evidences of enteritis, for Busse¹² has shown that the presence of typhoid bacilli in the blood stream do not necessarily give rise to enteritis or, for that matter, to agglutinating powers toward the bacilli. On the other hand, there is considerable evidence to show that in acute typhoid enteritis the bacilli may reach the gall-bladder from the duodenum. That typhoid ulceration may occur in the duodenum and stomach cannot be doubted. Such an instance of perforation of a typhoid ulcer in the duodenum occurred in the practice of my colleague, Dr. L. C. Grosh, in 1907.

After an attack of typhoid the infection may remain latent in the gall-bladder or in the alimentary or urinary tract for periods of years. In fact, with an earlier typhoid history, it is improbable that an acute exacerbation of latent cholecystitis is anything else but the result of the earlier infection. Levy and Kayser¹³ found typhoid bacilli at autopsy in the gall-bladder of a patient who had no symptoms of cholecystitis, but who had had typhoid fever three

⁵ Münch. med. Woch., 1888, p. 315.

⁶ Präger med. Woch., 1893, p. 1.

⁷ Johns Hopkins Hosp. Bull., 1898, ix, 91.

⁸ Mitteilungen a. d. Grenzgebieten d. Med. u. Chir., 1900, p. 389.

⁹ Verhand. d. Deutsch. patholog. Gesellschaft, 1907, xi, 143.

¹⁰ Ibid., xi, 150.

¹¹ Verhand. d. Deutsch. patholog. Gesellschaft, 1907, xi, 160.

¹² Münch. med. Woch., 1908, lv, No. 21.

¹³ Ibid., 1907, liii, No. 50.

years previously. Grimme¹⁴ has reported the case of an insane patient who was isolated because of the presence of typhoid bacilli in the stools, and from whom numerous gallstones were removed at operation. After an interval following the operation, typhoid bacilli were no longer found in the stools. Hammond¹⁵ found typhoid bacilli in the gall-bladder one year after an attack of typhoid. Hamilton,¹⁶ who investigated 24 individuals with history of gall-bladder disease, found that 2 were typhoid bacillus carriers and 5 paratyphoid carriers. Fromme¹⁷ has reported 4 cholecystectomies in 4 women typhoid carriers in all of whom elimination of bacilli ceased following the operation. Billings¹⁸ has described the conditions present in a contact carrier who gave a positive Widal reaction and from whose stools a pure culture of typhoid bacilli was obtained. Upon operation for cholecystitis, calculi and typhoid bacilli were found.

Holmes'¹⁹ recent article on the subject also shows that cholecystitis due to typhoid bacillus can occur, as in one of Cushing's²⁰ patients, without the history of an earlier attack of typhoid. Such patients must be considered contact carriers. In Holmes' patient the bacilli disappeared from the bile and stools in eight weeks following cholecystostomy. Holmes has very properly brought up the point that the mere presence of typhoid bacilli in the gall-bladder is not of itself sufficient to provoke the clinical symptoms of cholecystitis. It is only when the cystic or common duct is obstructed, during perhaps an otherwise latent period of the gall-bladder infection, that symptoms manifest themselves which we recognize as the clinical evidences of cholecystitis.

In most chronic carriers the bacilli are eliminated with the feces; in a smaller number the urine contains the bacilli. Forster believes the gall-bladder to be the site of continued reproduction of the bacilli which are intermittently ejected into the intestine. The Ledinghams uphold this view, since investigations have shown that the bacilli may disappear during the convalescent period of the disease only to reappear several months later, following perhaps, the administration of some cholagogue cathartic as suggested by Reitter.²¹

THE HISTORY OF TYPHOID BACILLUS CARRIERS. Experience has shown that, in most cases, the discovery of typhoid carriers has arisen from hitherto unexplainable endemic outbreaks among the inmates of asylums, or among families who have happened to

¹⁴ Münch. med. Woch., 1908, iv, No. 1.

¹⁵ Jour. Amer. Med. Assoc., January 2, 1909.

¹⁶ Ibid., February 26, 1910.

¹⁷ Deutsch. Zeitschr. f. Chirurg., 1910, cvii, No. 6.

¹⁸ Trans. Amer. Med. Assoc., June 27, 1911; abst. Medical Record, New York, 1911, lxxx, No. 1.

¹⁹ New York Med. Jour., August 12, 1911.

²⁰ Loc. cit.

²¹ Wien. med. Woch., 1908, p. 519.

employ the same cook, or obtained milk from a dairy previously under suspicion. A large number of typhoid carriers, in the sense that they have been the cause of such endemics, have been women who were, in some way, connected with the handling of food products. On the other hand, many carriers exist who, rather from good luck than good management, do not happen to infect others. Any individual who has been in contact with the disease, or who has himself suffered an earlier infection, may be a carrier in the sense that pure cultures of the bacilli may be obtainable from the stools or urine. Probably not more than one-half of such carriers actually infect others, although no definite data is available on this point, since the matter of cleanliness in personal habits varies, as a rule, with the social status of the individual.

Until the recent communication of Young, mentioned below, the largest number of recorded cases originating from one source was reported by Lumsden and Woodward,²² who found a typhoid carrier in a dairy responsible for 54 cases of the disease among the dairy customers. This carrier had had her attack eight years before. The time element since the original typhoid attack has been found to vary greatly. Gregg²³ has reported the case of a boarding-house mistress, who served as the source of infection in 7 cases of typhoid, fifty-two years after her own recovery. No bacilli were found in the blood or urine, but pure cultures were obtained from the feces. Jundell²⁴ has described the conditions present in a family, the grandmother of whom was known to be a typhoid carrier for fifty-four years, and during this interval 22 members of the family were attacked. This carrier was eighty-three years old, and her feces were found to contain typhoid bacilli.

Scheller²⁵ has described an endemic in Prussia in which during a period of fourteen years, 32 cases of typhoid were traceable to a woman employed in a dairy whose attack had occurred seventeen years previously. Typhoid bacilli were found in her stools in pure culture. Out of 40 people who drank the milk of this dairy, 18 were found to be carriers of the infection, and yet only 5 of the 18 had ever had typhoid. In other words, 13 were contact carriers. Soper's²⁶ painstaking investigation of so-called "Typhoid Mary," a contact carrier, showed that in ten years, 26 cases of typhoid could be traced to her as cook in households where the disease appeared. Typhoid bacilli were found in the stools, but none in the urine.

Young,²⁷ Commissioner of Health, of Chicago, in a personal

²² Jour. Amer. Med. Assoc., March 6, 1909, p. 749

²³ Boston Med. and Surg. Jour., July 16, 1908.

²⁴ Hygien. Festband, 1908; abst. edit. Jour. Amer. Med. Assoc., January 30, 1909, p. 388.

²⁵ Centralbl. f. Bakteriöl, 1908, No. 5, p. 385; abst. edit. Jour. Amer. Med. Assoc., June 13, 1908, p. 1986.

²⁶ Jour. Amer. Med. Assoc., June 15, 1907.

²⁷ Personal Communication, July, 1911.

communication, has recently described the conditions which resulted from the employment of a young woman in one of the suburban dairies. In June and July, 1911, three years after her apparent recovery from typhoid, 56 cases of typhoid were found in families receiving their milk supply from this dairy. To July 21, 1911, 4 deaths had occurred among this number. Negative bacteriological results were obtained in the study of the bowel and bladder discharges of all individuals connected with the dairy, except in the case of the young woman above mentioned. Part of her duty was to wash the milk cans. Nieter and Liefmann²⁸ found 7 carriers among 250 inmates of an insane pavillion where typhoid was endemic. At the autopsy of 1 patient who succumbed to chronic dysentery, typhoid bacilli were found in the intestines and in pure culture in the gall-bladder. The serum of this patient would agglutinate the typhoid bacillus in dilution 1 to 50, and the Flexner dysentery bacillus in dilution 1 to 100. After isolation of the carriers, the endemic ceased. Busse²⁹ was able to locate typhoid bacilli from the blood of 4 carriers who died of intercurrent diseases. Hutchinson³⁰ has reported the career of a lodging-house keeper whose attack occurred fifteen years earlier and who was responsible for 7 cases of typhoid. Similar investigations have been made by the Ledinghams,³¹ by Connell,³² Huggenberg,³³ Southward,³⁴ Dehler,³⁵ Nieter,³⁶ Branthwaite,³⁷ and by Madsen.³⁸

DIAGNOSIS. It will be obviously impossible to keep any large number of typhoid convalescents under bacteriological surveillance. As mentioned in an earlier article³⁹ popular education may be of service in dealing with the problem. This education can best be carried on by physicians who should bear in mind the possible connection between an earlier attack of typhoid, or the possibility of infection by contact, and symptoms, sometimes slight, referable to the gall tract, to a slight urinary cystitis, or bacteriuria, to chronic colitis, to mild dysentery, or to attacks of so-called intestinal indigestion. The source of endemic outbreaks should be investigated whenever possible, and the possibility of direct infection of food products by a typhoid bacillus carrier should be borne in mind. Surgeons should have cultures taken in all operations involving the gall-bladder, and physicians at the time of their examinations

²⁸ Münch. med. Woch., 1906, liii, No. 33.

²⁹ Loc. cit.

³⁰ Brit. Med. Jour., March 26, 1910.

³¹ Ibid., January 4, 1908; *ibid.*, October 17, 1908.

³² AMER. JOUR. MED. SCI., 1909, cxxxvii, 637.

³³ Correspbl. f. Schweiz. Aerzte, 1908, xix, 635.

³⁴ Archives of Pediatrics, March, 1907.

³⁵ Münch. med. Woch., 1907, liv, No. 16; *ibid.*, 1907, liv, No. 43.

³⁶ *Ibid.*, 1907, liv, No. 33.

³⁷ British Government Report, *abst. Jour. Amer. Med. Assoc.*, April 4, 1908.

³⁸ Hospitalstidende, Copenhagen, 1910, liii, No. 14; *abst. Jour. Amer. Med. Assoc.*, June 25, 1910.

³⁹ Jour. Amer. Med. Assoc., 1910, lv, 1708.

should search for post-typhoidal sequelæ in those who have had the disease, and for contact carriers through association, in those who deny previous infection. Such sequelæ are especially apt to be found among patients presenting evidences of gall-bladder disease, the symptoms of which are frequently referred to the stomach. In fact, all patients showing evidences of gall-bladder disease, whether months or years after a history of typhoid, should be considered as possible chronic typhoid carriers until proved otherwise.

Cultures should be taken in all post-typhoid cases whose urine contains bacteria. Likewise cultures should be taken from the stools in all cases showing symptoms of chronic dysentery or colitis. The colon bacillus will practically always be obtained from the stools, and may be confusing, but the typhoid bacillus, if present, can be isolated from the plates with comparatively little difficulty. The diagnosis will depend upon the isolation of a bacillus which gives culturally the main characteristics of the bacterium of Eberth. That is to say, a short motile rod which grows rapidly in bouillon or on agar slant, which does not liquify gelatin nor produce indol or coagulate milk, nor produce gas or acid in glucose litmus gelatin, and produces an invisible growth on potato.

It is the personal conviction of the writer that these main characteristics are not given by all strains of typhoid bacilli, for in 1 of the 3 cases studied during the past two years the cultural findings were confusing. In one (C. R. D.) who had never had typhoid and who was regarded as a contact carrier, the pure cultures obtained from the urine throughout a long period of treatment, would at times correspond to the main cultural characteristics mentioned, while again slight amounts of gas and acid would be produced in the media. In this connection it may be worth mentioning that no symptoms of cystitis or pyelitis were present in this patient. He was referred for examination because of the constant presence of enormous numbers of bacteria in the urine. During many months of treatment no pus cells were found, a condition seldom, if ever seen, when the colon bacillus is the causative organism.

In other words, the colon bacillus when present in the bladder produces an inflammatory reaction which is recognized as a true cystitis, while the typhoid bacillus when present in the urinary tract, in typhoid carriers is eliminated in suspension in the urine, a condition recognized as bacteriuria. Still further proof, in support of the view that this patient was a typhoid carrier, is afforded by the fact that he failed to react to the treatment ordinarily successful in dealing with colon bacillus infections of the urinary tract; that is, the use of hexamethylenamine and sodium benzoate internally and the use of a colon vaccine. It may be mentioned also that his blood serum would agglutinate, in dilution 1 to 50, a stock typhoid culture. He was not benefited by inocu-

lations of an autogenous vaccine, and gave up treatment before inoculations of a stock typhoid vaccine were begun.

The agglutinating power of the blood serum as well as the phagocytic power is found to be increased in typhoid bacillus carriers, as a rule, while the bactericidal and bacteriolytic powers are below normal. This is in accord with the previously expressed opinion that such individuals are but partially immune, since it has been shown^{40 41} that normally during convalescence from the disease, the bactericidal and bacteriolytic properties of the serum are increased to the point of destruction of the bacilli. These facts are of value in the bacteriologic study of a suspected individual and may be of service from a diagnostic standpoint. Alice Hamilton⁴² has also shown that carriers have a persistently high opsonic index and relatively high agglutinative power; that is, their immunity is phagocytic, not bacteriolytic, or bactericidal.

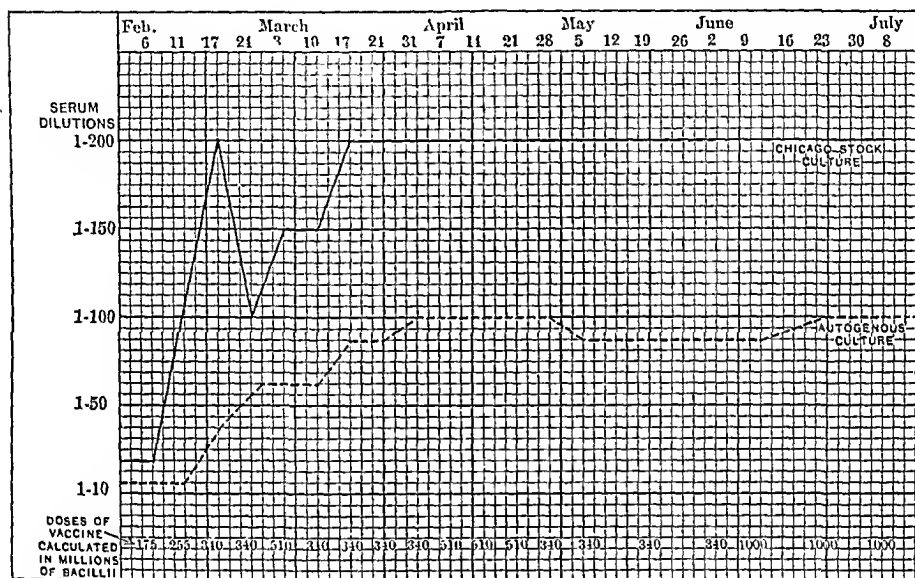
REPORT OF A TYPHOID CARRIER AND VACCINE TREATMENT. R. F. (record 565), aged twenty-eight years, from Deerfield, Michigan, was referred by Dr. R. M. Eeles, January 17, 1911, as a possible typhoid carrier, although no cases of the disease were traceable to him. In 1904 this patient had typhoid fever for six weeks with apparent recovery for one year, after which time he began to complain of pain in the region of the umbilicus which continued until 1909. The subsequent history was supplied by Dr. Geo. Sellards, of Deerfield. In 1909, diarrhea began; the bowel discharges numbered five or six daily with some mucus, and in December, 1909, three severe hemorrhages from the bowel occurred, with temperature as high as 104°. The last hemorrhage measured over one quart. The diarrhea continued for one year thereafter. The discharges were occasionally streaked with blood and mucus but gradually subsided under medication. The weight before the attack of typhoid seven years ago was 151. At the time of examination it was 134. He complained of frequent headaches. The examination revealed nothing of importance on the part of the heart, lungs, nervous system, and abdomen, except some tenderness on pressure was present below the umbilicus. One loose stool occurred every morning, with poor control of the sphincter ani. Examination of the fresh stool for *Amebæ dysenteriae*, as well as stains of the mucus present for tubercle bacilli were negative. The von Pirquet skin reaction was negative. The leukocytes numbered 7200, and the urine was negative to albumin, pus, and sugar. There had never been any urinary symptoms. The Adler occult blood test was positive in the stools. Cultures taken from the stools showed the presence of the colon bacillus and a short, plump, actively motile rod, which in pure culture, did not produce

⁴⁰ Proc. Royal Soc., 1903, and Jour. Royal Army Med. Corps, 1907 and 1908.

⁴¹ Jour. Amer. Med. Assoc., 1909, liii, 1253.

⁴² Loc. cit.

acid in litmus gelatin, or gas in stab culture on glucose agar, nor was indol produced after ten days growth in bouillon. Milk was not coagulated. The agar slant showed a growth which resembled that of the typhoid bacillus, while the growth was invisible on potato. Gelatin was not liquefied in six weeks. Cultures from the urine showed a few isolated colonies of *Staphylococcus albus* (probably contamination). Subsequent cultural studies of the fresh stool gave the same findings. His blood serum would agglutinate a stock typhoid culture in dilution 1 to 20, while the autogenous strain would agglutinate in dilution 1 to 10.



Mr. R. F., aged twenty-eight years. Chart shows the increase of the agglutinating power of his serum for the bacillus of Eberth under injections of autogenous typhoid vaccine.

A vaccine was prepared from the typhoid organisms present in the stools. He received his first inoculation on February 6, 1911. Between that date and May 5, 1911, fourteen inoculations were given at weekly intervals, the doses varying between 110,000,000 and 510,000,000. Negative cultures were obtained in May, 1911. Since that time he has received five additional inoculations, three of which have contained 1,000,000,000. The agglutinating power of the patient's serum was increased ten fold during the course of treatment. Coincident with the vaccine treatment and the increase in the agglutinating powers of his serum (see Chart) his general condition improved. The tendency to loose stools with poor sphincter control disappeared and the bowel discharges became normal in appearance and gave negative cultures. He was discharged July 8, 1911.

THE MEDICINAL TREATMENT AND CONTROL OF TYPHOID CARRIERS. The problem is a perplexing one, since the installation of adequate filtration plants and careful dairy supervision will not, for years to come, rid most American municipalities of typhoid. In most localities the disease has been endemic for years with a consequent large number of unrecognized carriers. Such individuals if employed as cooks, waiters, and waitresses, dairymen and dairymaids, workers in confectionery, hucksters, workers in artificial ice plants, or in any capacity which requires the handling of food products may continue to serve throughout long periods of time as a menace to the public health.

Since the treatment of such individuals has not been uniformly successful, the question immediately arises as to what steps local and state boards of health should employ to protect the public. For example, in the recent Chicago outbreak, 56 cases of typhoid with 4 deaths have resulted from the uncleanly personal habits of a young woman employed to wash the milk cans in the dairy. What other attitude could or should be taken by the Municipal Department of Health except to employ its police powers toward the isolation of such an individual for treatment. Although innocent of harm she has been directly responsible for 4 deaths to date, to say nothing of the invalidism and expense incurred by over 50 others. There is much to be said regarding personal liberty, but since the law gives protection to property, personal and real, it is only fair to assume that such protection should be given to the health of individuals who are well; an asset far greater than the asset of property. Progress in every walk of life depends upon those who are in good health, but strange to say, the wheels of progress turn slowly, and stranger still, our law-making bodies can be induced to attach relatively little importance to prophylactic medicine. However, the danger to the public health will be greatly minimized, if when typhoid bacillus carriers are discovered control could be exercised over them by the local boards of health, with the idea of securing proper treatment, and restricting them to employment which do not have to do with the handling of food supplies.

The treatment of the chronic typhoid carrier by so-called intestinal and urinary antiseptics, such as sodium phenolsulphonate, sodium salicylate, salol or hexamethylenamine, and sodium benzoate, has been of little avail. During convalescence from the disease when the natural immune bodies, such as the bacteriolysins and bactericidins, are augmented, such antiseptics are undoubtedly of value and should be employed in every case as an useful adjunct. Graham, Overlander, and Dailey⁴³ found that 23 per cent. of 65 typhoid patients showed typhoid bacilli in stools and urine for ten

⁴³ Boston Med. and Surg. Jour., January 14, 1909.

days before their discharge. An important lesson should be learned from these facts, since it is entirely probable that if the convalescence of typhoid cases was studied and treated with as much care as the active stages of the disease, the number of chronic carriers would be greatly lessened. During convalescence from the acute attack, when conditions are most favorable because of the natural augmentation of immune bodies, help may be secured by medicinal means; while in chronic carriers the bactericidal and bacteriolytic properties of the blood serum are decreased and such medicinal assistance as may be offered, is of little avail.

VACCINE TREATMENT. The number of typhoid carriers successfully treated by vaccines has not been large. Irwin and Houston⁴⁴ were able to cause disappearance of the infection in a patient who for seven years had been a carrier. She received during two months, five injections varying from 50,000,000 to 500,000,000. Meader⁴⁵ has also successfully treated a patient and found that the best therapeutic dose varied between 75,000,000 and 400,000,000. He has shown that the disappearance of the infection coincided with the increase in the bactericidal power of the blood serum of the patient. In my report⁴⁶ of a typhoid carrier treated during 1910, it was shown that the agglutinative, bacteriolytic and bactericidal properties of the blood serum were augmented during the course of six injections which varied from 100,000,000 to 400,000,000. The increase in the immune bodies of the serum was followed by the disappearance of the infection. Brem and Watson⁴⁷ have recently reported the case of a child, aged four and one-half years, whose urine was found to contain the bacilli a few months after convalescence. She subsequently received nine injections of autogenous vaccine in about two months, when the urine was found to contain no bacilli. The agglutinative powers of the patient's serum increased markedly to 1 in 1000 during the course of inoculations.

In fact, it may be said, that the treatment of carriers by inoculations of vaccine offers more hope for cure than any other known method. It probably is better to use a vaccine prepared from the patient's own organisms, although no definite proof exists that such is the case. The work of Leishman and his associates seems to prove that as efficient an immunity is conferred by a stock vaccine as by an autogenous vaccine, and that a single nonvirulent strain is capable of producing as efficient an immunizing response as vaccine prepared from single or multiple virulent strains. The method of dosage found to be most satisfactory has been to increase gradually from 100,000,000 to 1,000,000,000 depending upon the

⁴⁴ *Lancet*, London, January 30, 1909. ⁴⁵ *Johns Hopkins Hosp. Bull.*, September, 1910.

⁴⁶ *Loc. cit.*

⁴⁷ *Trans. Amer. Med. Assoc.*, June 27, 1911; *abst. Medical Record*, New York, 1911, lxxx, No. 1.

evidences of immunizing response as obtained by study of the agglutinating, bactericidal, and bacteriolytic power of the blood serum.

The vaccine should be prepared as follows: Pure cultures of the organisms are grown on agar for twenty-four hours, when the growth is washed off with sterile salt solution. The resulting suspension is thoroughly shaken to break up the clumps and a small quantity drawn into an ordinary red blood pipette, diluting 1 to 200, with salt solution for purpose of standardization. A small drop of this dilution is then placed upon the *blood-platelet* counter of Zeiss. The *blood-platelet* counter differs from the ordinary red blood cell counter in that with the former, the depth of the chamber is only $\frac{1}{50}$ mm. Twenty-five small fields are counted under the microscope, using dim direct illumination or indirect illumination by the dark-field condensor, and the sum divided by twenty-five to obtain the unit value. The unit value is then multiplied by the dilution, by the depth of the chamber, by 400, the number of small squares in a millimeter, and, lastly, by 1000 to convert to cubic centimeters. For example, if fifty bacterial cells are counted in twenty-five small squares, the unit value per square would be two, multiplied by 200, by 50, by 400, and by 1000, or 8,000,000,000, the number of bacteria per c.c. of suspension. The suspension is then heated to 54° to 55° C. for one hour in a sealed test-tube, in a water bath and then diluted with sterile salt solution, containing 0.35 per cent. phenol, so that each cubic centimeter of the finished vaccine contains approximately 1,000,000,000. Care must be exercised not to overheat the vaccine, since overheating impairs its immunizing properties. The thermal death point of most strains of typhoid bacilli varies between 53° and 56° C. Cultures should be taken from the vaccine to insure sterility before using.

CONCLUSIONS. 1. Not only should individuals who are typhoid carriers receive appropriate vaccine treatment, but all individuals including physicians and nurses, whose duties require the attendance and care of typhoid cases should receive immunizing treatment. By this procedure many individuals otherwise destined to become chronic carriers might secure protection which would prevent in themselves the possibility of cholecystitis or other late manifestations, as well as avoid the possibility of becoming a source of danger to others.

2. Such treatment has been found efficient and productive of little discomfort. Nurses, orderlies, and physicians should be regularly immunized at intervals of two or three years, as should all others exposed to endemic or epidemic outbreaks.

3. When typhoid bacilli have produced clinical or bacteriological evidences of cholecystitis, it is doubtful whether vaccine treatment will of itself be of avail, surgical drainage of the viscus then being indicated. On the other hand, appropriate vaccine treatment in

individuals showing evidences of intestinal or urinary tract perpetuation of the bacilli, without cholecystitis, during convalescence from the disease or subsequently, should be given the opportunity of vaccine treatment. Not all will be cured but the bacilli will disappear in some instances.

4. Chronic carriers who have been unsuccessfully treated by vaccines should be under the control of the local board of health and furnished employment if necessary which would not require the handling of food products.

EPIDEMIC POLIOMYELITIS: A CLINICAL STUDY OF THE ACUTE STAGE.¹

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It is an interesting fact, that although our knowledge of acute poliomyelitis dates back over seventy years, when the German surgeon, Jakob Heine² first described it under the name of "the spinal paralysis of children;" the true nature of the disease, its pathology, clinical manifestations, prognosis, infectiousness, contagiousness, have only lately been fully ascertained, and have, only in the last decade, become the subject of general knowledge. Furthermore, it is of interest to note that at the same time that Heine first made his observations in Germany, an American practitioner, Dr. Colmer, observed a small epidemic in Louisiana, and recorded it in the AMER. JOUR. MED. SCI. (1843, v, 248). Little or nothing was added to the knowledge of the subject for the next thirty years. No epidemics were reported until 1881, when 18 cases occurred in Sweden. Subsequently, epidemics were reported from Norway, Sweden, Germany, the United States, and Canada, in the eighties and nineties. The most extended epidemics occurred in the above-named countries in the last five or six years.

A noteworthy contribution was made by Strümpell³ in 1885, in his paper on Poliencephalitis Acuta in Children. Pathologically and clinically this disease was noted as identical with the well-known forms of spinal poliomyelitis. For the first comprehensive clinical studies we are indebted to the Danish physicians Medin⁴ and Wickman.⁵ Aside from his contributions to the pathology, Wickman was able to show conclusively, that the disease is contagious.

¹ Read before the Metropolitan Medical Society, Academy of Medicine, October 24, 1911.

² Die spinale Kinderlähmung, 1810 and 1860: a study of 150 cases.

³ Jahrb. für Kinderheilk., 1885, Band xxii, N. F.

⁴ X. Internationaler Congress, Berlin, 1890.

⁵ Beiträge zur Kenntniss der Heine-Medinschen Krankheit, Berlin, 1907.

Pathologically speaking, the disease has been characterized as a meningo-encephalo-polio-myelitis. Of late, it has been shown, however, that the lesions are not confined to the gray substance of the brain and cord, but may be found in the contiguous white substance, as well as in parts which have no direct communication with the gray matter.

Recently the study of poliomyelitis has entered into a new phase through its successful inoculation into monkeys.

In taking up this subject of poliomyelitis I wish to dwell mainly on its diagnostic features. If this be an infectious and contagious disease, as now seems certain, our duty as practitioners clearly lies not only with the patient, but also with the family and the community. Aside from the fact that the recognition of its inception is of great importance on account of the dubious prognosis as to life and limb, it is clearly our duty to diagnosticate it as early as possible, in order to prevent its transmission to others.

After a careful study of the manifold clinical manifestations leads up to a diagnosis of the case, the question of prognosis is the all important consideration. Having this in view, I would therefore, propose the following classification, which, empirical though it may seem, is comprehensive, and tends toward a practical purpose. Poliomyelitis can be divided into: (1) The abortive cases, mild or severe in their onset or course, which end in complete restitution in a short time; (2) cases with paralyses, these may end in complete restitution or in partial or complete atrophy; (3) the rapidly fatal cases (*formes frustes*). This classification has some value, because it covers the whole ground and lays equal stress on the mild, transient forms, as well as on the paralytic and the fatal cases, putting the former on a par with the well-known paralytic forms.

By this classification I mean to lay stress on the fact that a large number of abortive cases pass unrecognized at the present time, while, judging from our experience of other infectious diseases, these same abortive cases spread the epidemic. Observations made during epidemics of poliomyelitis seem to show that the group of cases occurring not infrequently in infants and young children, hitherto styled meningitis serosa, as well as certain unclassified spastic or tetanic affections of childhood may well belong to the abortive type of poliomyelitis. This also holds good for certain unexplained fatal cases in children and adults. How large their number is, however, cannot at present, be estimated.

What means are at our disposal at the present time to recognize with any degree of certainty a case of acute poliomyelitis? What are the characteristic symptoms of the disease; what additional diagnostic aid does the laboratory offer toward making a positive diagnosis?

In studying the literature of the extended epidemics of Sweden, Norway, and Germany, it becomes at once apparent that the recognition of cases, even though they may be atypical in their clinical manifestations, seems comparatively easy. The existence of a widespread epidemic has been officially noted, the authorities are on the alert for every case, the practitioner is instructed to watch for and report all suspicious cases. An organized medical campaign is thus established in the country districts, the hamlets, villages, and small towns, and the progress of the epidemic can be followed from house to house.

In a city like New York, for example, conditions are totally different. It is true that we are forewarned that the epidemic generally appears in the summer months, and, furthermore, we know that the disease has become endemic with us. Thus, sporadic cases make their appearance at any time, and must be recognized without the aid of epidemiological data. If the cases are brought in from the country, it is sometimes possible to determine the existence of an epidemic in that outlying district. If the case is not an extraneous one, a clue as to its origin and transmission, in the city proper, can usually not be obtained, thus the etiological factor does not become apparent, and the possibility that one is dealing with a case of poliomyelitis is not even thought of or considered. Nothing would be of greater aid to the practitioners of large cities than the daily publication in the public press, by the Board of Health, State or National Health Boards of the daily number of cases of infectious and contagious diseases. In this way the family doctor would be apprised of the existence, the increase and decrease of the various epidemics, and exact information on these points would materially aid him in the diagnosis of suspicious cases.

Since Medin's time, clinicians are wont to look for the predominance of certain irritative and paralytic symptoms of the nervous system, to aid them in recognizing the disease in its various forms. Aside from the abortive cases, which may present themselves under the most varied guise, the principal types of poliomyelitis are: The spinal, meningeal, cerebral, encephalitic, bulbar, and pontine, Landry's ascending and descending paralytic, the polynuritic, and the ataxic types. It goes without saying, that these various types may overlap or combine. There is no room for doubt, that the systematic subdivision into the above-named groups, indicating as they do, the seat of the lesion, lend material aid in the diagnosis of poliomyelitis in its paralytic stage. In the acute stage, however, they only serve the purpose of indicating the existence of some infectious process in the cerebrospinal system, the nature of which must be especially determined. In other words, our method of diagnosis, at the present time, is a purely empirical one, and will remain so, until the diagnosis can be made from the secretions or excretions, from the blood or spinal fluid, bacterio-

logically, serologically, or by other exact biological methods. Our method of diagnosis, then, being purely empirical it is just as important to note certain other symptoms, which, though they may vary in different epidemics, must be carefully considered, as they are present at the very inception of the attack and may cover up or disguise the true nature of the underlying affection. A poliomyelitis may begin with or run its course under the form of an angina, tonsillitis, influenza, a gastro-enteritis, a rheumatic fever. In some epidemics most of the cases were accompanied by the various respiratory and intestinal symptoms of acute influenza. Indeed, a Swedish author⁶ has attempted to show that poliomyelitis is only a form of influenza infection, although he has failed to demonstrate the constant presence of the bacillus of Pfeiffer in his cases. Angina and tonsillitis are often seen in the prodromal stage, or are the concomitant symptoms of the early acute stage. Again, the gastro-intestinal tract seems to be the principal seat of the infection in some epidemics, and the disease runs its whole course under the mask of a diarrhea accompanied with fever. The description of such a case is given below. When these cases occur in an abortive form, it is doubtful whether they can be recognized at all, especially in infants and young children, unless a careful search is made for symptoms of irritation of the brain and cord.

THE ABORTIVE CASES, THEIR DIAGNOSIS AND SIGNIFICANCE. Our knowledge of the abortive cases of poliomyelitis only date back to the observations of Wickman⁷ made in the great Swedish epidemics of 1905 and 1906. He holds that they are frequent, probably exceeding in number the paralytic cases. As they have hitherto only been recognized when they occur in connection with typical cases, it follows that the number of abortive cases is much greater than is ordinarily supposed. Their epidemiological importance cannot be overestimated. Wickman cites a large series of family infections, in which abortive cases occurred in connection with paralytic cases of varying intensity, together with fatal cases. Some of the children after a short feverish attack were well in a few days or a week, and returned to school. Accordingly, the abortive cases are the principal carriers of the infection.

In my service at the German Hospital, in September, 1910, an abortive case of poliomyelitis of the gastro-enteritic type came under my notice, which was not recognized during its course, but was subsequently proved to belong to this group, through the kind interest of Dr. Simon Flexner. The case was published in the *Medical Record*, of July, 1911. As it is very instructive, I will mention it here, somewhat in detail:

⁶ Th. Brorström, *Akute Kinderlähmung und Influenza*, Leipzig, 1910.

⁷ *Die akute Poliomyelitis*, Berlin, 1911.

CASE I.—J. W., aged six years, entered the Hospital September 4, 1910, discharged cured, September 21, 1910. Diagnosis, acute dysentery, meningism. His father was living. His mother died of consumption. He had measles in February, 1910. For the several weeks before admission he had been restless at night. On September 3, at noon he was seized with a chill, then complained of headache, which gradually became very severe. He became drowsy, then unconscious, and had vomiting and diarrhea.

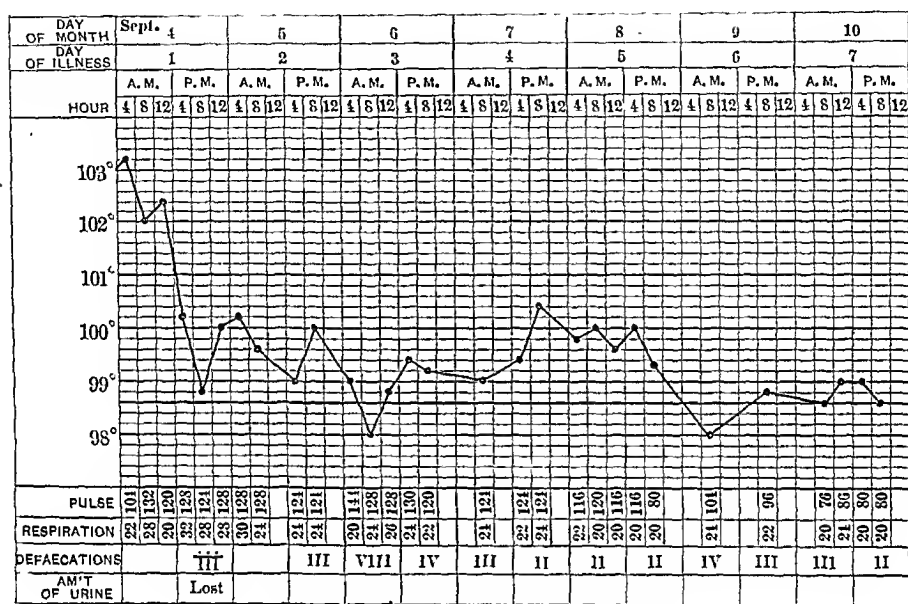


CHART 1.—Case I. Abortive poliomyelitis.

Examination. The patient was somnolent but responded if aroused. There was rigidity of the neck and tenderness of spine. The eyes, ears, nose, were negative except for myosis and tardy reaction of the pupils to light. The abdomen was negative, the spleen was not enlarged. There was a slight Kernig and Babinski of both lower extremities, other reflexes were normal. The highest temperature was 103°.

The case ran the course of an acute dysentery; the stools contained mucus and blood. The urine was negative. Gradually the nervous symptoms became more marked; opisthotonos, delirium, and extreme restlessness developed. A clear fluid escaped under moderate pressure from a lumbar puncture. The number of stools diminish, the temperature and pulse became normal in the course of a week. The symptoms of meningism subsided. The reflexes were never absent at any time.

Although meningism occurs as a symptom of various infectious diseases, especially in children, our original interpretation

of the case did not seem wholly satisfactory, especially after hearing of several cases of poliomyelitis of the gastro-enteritic type which had occurred in the course of the summer. On looking up the patient at his home, a careful examination of his reflexes showed no anomalies. There were no paralyses of any kind. Two ounces of blood were taken from the arms of the patient and subjected to the neutralization test.

This test is made by mixing for many hours, the active virus derived from apes with the serum of an immunized human being, and injecting it intracerebrally in apes. Controls receive in the same manner, virus mixed with the serum from an individual who never had anterior poliomyelitis. The controls contract the disease, while the test cases escape, presumably because of the antibodies present in the immunizing serum. The test in our case showed a positive result. As there was nothing in the patient's previous history pointing to an attack of poliomyelitis, we had doubtless been dealing with a case of the abortive type of this disease.

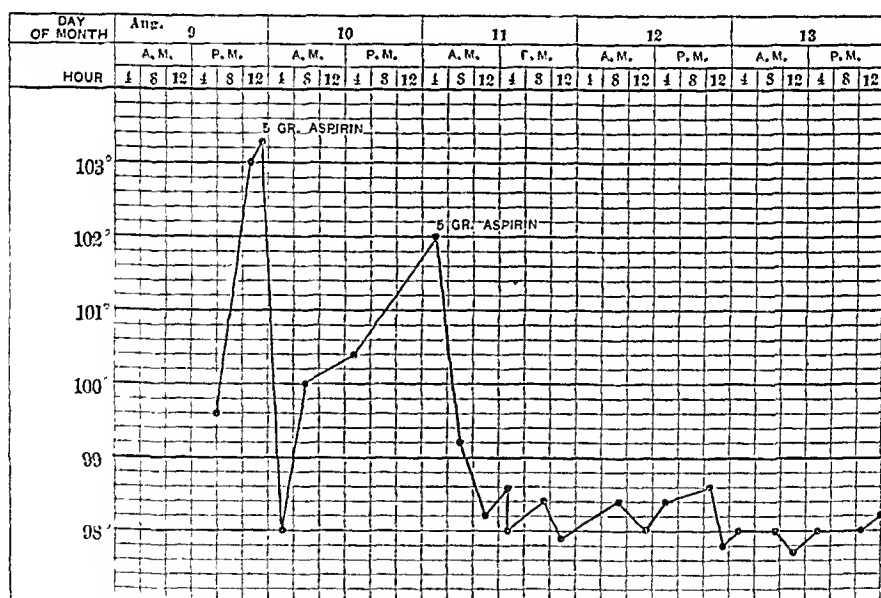


CHART 2.—Case II. Abortive poliomyelitis (meningism).

CASE II.—Since then another case came under my notice and partial observation which allows of the same interpretation. A family with a number of children, travelled through Norway, Sweden, Germany, and France. While in Norway, one of the children had a mild attack of tonsillitis. He subsequently complained of being very tired. Two weeks after leaving Norway, the child complained of headache, which gradually became so

intense that he could not bear his head to be touched, and had to lie down. On the second day, the temperature gradually rose to 103°, pulse, 108. There were no gastro-intestinal symptoms nor cough. The patient gave the impression of being very ill, was extremely irritable, and when he awoke from a restless sleep, complained of severe headache. The pupils were small, but equal, and reacted to light slowly. The patellar reflexes could hardly be elicited, and no Babinski or Kernig phenomena were present. The cremaster and abdominal reflexes were present and equal. There was stiffness of the neck and inability to put the chin on the chest. A tentative diagnosis of cerebrospinal meningitis was made and a doubtful prognosis was given. In the course of the fourth and fifth day, however, the meningitic symptoms gradually disappeared, and the child made an uneventful recovery. Six weeks later, the left patellar reflex was present, the right one absent. There seemed to be a slight paretic condition in the distribution of the right facial nerve. Examinations in the seventh, eighth, and ninth weeks after the attack showed that the patellar reflex of the right leg was gradually becoming normal. This was undoubtedly a case of abortive poliomyelitis.

CASE III.—A child, aged three and one-half years, was brought to the German Hospital, August 30, 1911, with a history of fever and diarrhea for a number of days. The mother said the child was unable to stand or walk alone.

Examination. With the exception of a slight rise of temperature, and a number of diarrheic movements, the child, as it lay in bed, did not present anything worthy of note. On placing the child on the floor, however, it could not rise, the feet seemed flabby, the big toes bent under the feet. In a sitting or standing posture, when held by the arm, the trunk reclined to the left side. The pupils and face were normal. The right patellar reflex was diminished, the left normal. Abdominal and cremaster reflexes were present and equal. The electrical reaction of the affected muscles of trunk and extremities were normal. In two weeks after treatment by urotropin, baths, and electricity, the child was able to walk. At the present time there is a distinct limp of the right leg and the patellar reflex on the right side is diminished.

Cases like Case III are not uncommon I presume. On account of the shortness of the febrile stage, they first come under observation when paralysis has set in, and pass on to partial or complete restitution or complete paralysis, according to the severity of the lesions in the anterior horns and surrounding nerve tissue. Frequently, the orthopedist is the one who first sees these cases, as occurred in the following case.

CASE IV.—A perfectly healthy but very neurotic girl, aged eight years, complained of headache and dizziness, but insisted on going to school. During the night the child's temperature

rose to 103° ; she complained of headache, pain, and heaviness in the lower extremities. On the following morning the mother was thrown into a frenzy, because the child could not sit up or move her legs and had slight difficulty in passing urine. Both patellar reflexes were absent. The temperature was normal on the fourth day, and remained so. Examination showed that the peroneal group of muscles of both limbs were affected, also the posterior tibial muscles, more on the right than on the left side. This case was treated by Dr. J. Teschner with exercises and reëducation. The child never made use of a crutch, nor was a splint applied. She now walks with the characteristic swing and drag of infantile paralysis.

CASE V.—This was a healthy, well-developed boy, aged sixteen years, seen in consultation last summer. He had returned from the Adirondacks, with the history of remittent temperatures for three days. The patient complained of heaviness in the lower extremities and pain in the back. An incubation history could not be obtained. Patellar, cremaster, abdominal reflexes were present, equal and slightly exaggerated. There was a distinct Kernig's sign in both lower limbs. The pupillary reaction was normal to light and accommodation. There was slight stiffness of the neck. The spleen was not palpable. There was no bradycardia, the temperature was about 103° . Leukopenia and relative lymphocytosis were present. The Widal reaction was negative. The possibility of typhoid fever or cerebrospinal meningitis was considered. A spinal puncture, however, gave a clear fluid, containing 90 per cent. of lymphocytes. Subsequently, partial flaccid paralysis of the extremities followed. This was a typical case of the spinal form of poliomyelitis.

CASE VI.—S. F., a girl, aged about five years, whose mother was tuberculous, was suddenly seized with tonic and clonic convulsions. The patient moved both arms and legs convulsively or held them in tonic flexion; at times the arms and legs were relaxed; then again the legs were held in hyperextension. This was accompanied by twitching of the face, especially on the right side and rolling of the eyes. Severe opisthotonus occurred, which persisted for a number of days. All the reflexes were exaggerated. The pupils were unequal, Kernig's sign was present in both lower extremities, and there was a tache-cerebrale. Her temperature was steadily high, between 104° and 105° . After these irritative symptoms, the patient gradually lapsed into a comatose condition in which she remained for two or three days. During this period, stiffness of the neck and back persisted so that it was impossible to roll the child on her side, as she seemed to resist enforced motion. Spinal puncture was repeatedly made, a clear fluid showing small and large mononuclears escaped under pressure. There was occasional rolling of the hands inward, general tremor, and nystagmus.

feed himself. He was, however, able to move the elbow and wrist-joints, but muscular action of the arms was weak. No pains.

Examination. The patient was bathed in profuse perspiration, lay helplessly in bed; he was unable to sit up, as he could not support himself on his arms or hands. The eye muscles were normal and the pupils reacted normally to light and accommodation. There was stiffness of the neck, inability to move the head from side to side, or flex it on the chest, and moderate rigidity of the spine. No hyperesthesias. There was complete loss of motion at both shoulder-joints, yet extension of the forearms was accomplished promptly. The hands and fingers were readily moved. Considerable muscle weakness existed. There were no paresthesias or hyperesthesias, no special points of tenderness along the nerve trunks. The knee-jerks were not obtainable; Kernig, Babinski, and Romberg signs were absent, and there was no loss of function or weakness of the leg muscles. No disturbance in sensation or electrical reaction of either upper or lower extremities occurred. Lumbar puncture was dry. The patient acted peculiarly, screamed during sleep, talked irrationally, wanted to get out of bed. On September 11 he was slightly delirious, and had some difficulty with speech and swallowing. The patient died suddenly during the night. The autopsy showed hemorrhages in the upper part of cord and pons. This was a case of the bulbar and pontine poliomyelitis of Oppenheim and Erb.

CASE VIII.—Female child, aged two and one-half years. Bottle-fed, well nourished. In September, 1908, she had an attack of enteritis with fever. The child seemed very restless and nervous; complained of headache, and was suddenly seized with general convulsions which lasted for two days and nights. Chloroform was constantly administered. There was convulsive twitching of the face and tongue, with inability to swallow. The temperature was up to 105°. The pupils were contracted. Bilateral Kernig's sign was present. The abdominal and patellar reflexes were not exaggerated, and there was no foot clonus. Trousseau's sign was present. Spinal puncture gave a perfectly clear fluid. At no time was there stiffness of the neck. The irritative symptoms persisted about a week, then the upper and lower extremities gradually relaxed and the pupils became dilated. The patellar reflexes disappeared. It was observed that the child did not take notice of objects placed in front of it, or held before its eyes; an examination of eye grounds by Dr. Koller showed hyperemia of the retinal vessels, but no optic neuritis. The child had a flaccid paralysis of the lower extremities, and was unable to stand. The hands were held in flexion. No reactions of degeneration were present. As there was an extended epidemic of cerebrospinal meningitis at the time, the question as to whether we were dealing with this infection was also favorably considered. In view of the

fact, that opisthotonus was never present, that the spinal fluid was clear, and that the attack was ushered in by a severe enteritis which ran parallel with the nervous symptoms, I am inclined to uphold my diagnosis of encephalitis, in which I was supported by several competent observers. I would group this case with the encephalitic type of poliomyelitis, in the light of our present knowledge of this disease.

Observers of the meningeal and cerebral forms of poliomyelitis like Wickman⁸ and others go into a very careful differential diagnosis between this type of poliomyelitis and cerebrospinal meningitis. In exhaustive treatises⁹ of epidemic serebrospinal meningitis, however, the differential diagnosis of the two diseases is not even considered. From this I infer that the cerebral type of poliomyelitis has hitherto often passed unrecognized.

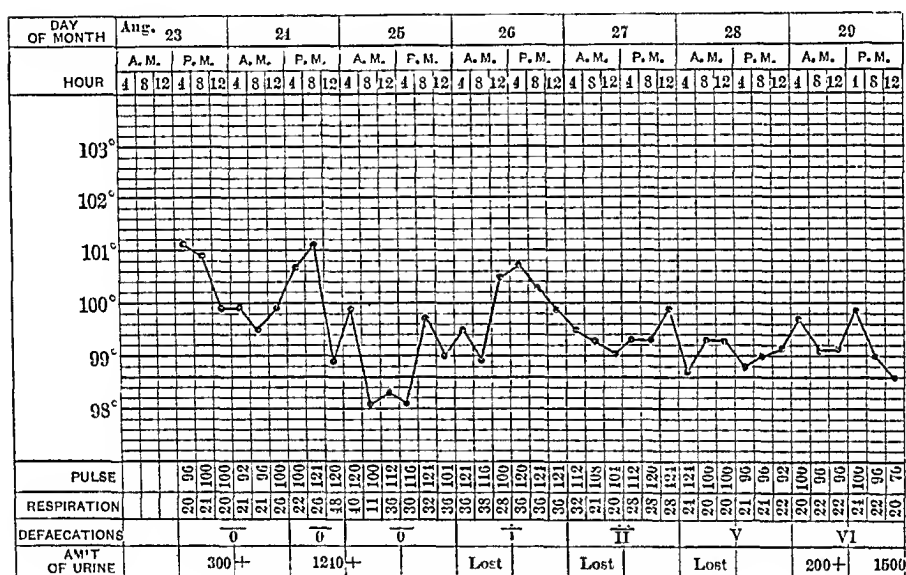


CHART 4.—Cerebral type of poliomyelitis.

CASE IX.—The following case is of interest in this connection. A native German, male, was brought to the hospital in a comatose condition on September, 1911. There was no history available excepting the fact, that he had come from the Catskills, where a few cases of infantile paralysis had occurred. Soon the patient was seized with tonic and clonic convulsions of the right side of the face, arm, and leg. Between the attacks the arms were held in fixed flexion. The right pupil was larger than the left. All

⁸ Loc. cit.

⁹ Goepfert Epidemic Cerebrospinal Meningitis (Genickstarre) Ergebnisse der Inneren Medizin und Kinderheilkunde, 1909, Band iv, p. 165.

the reflexes were exaggerated and were stronger on the right than on the left side. Foot clonus, Oppenheim and Babinski reflexes, were present on both sides. Abdominal and cremaster reflexes were intact. On stroking the plantar side of the right foot with the hammer a very strong contraction of the vastus of the right thigh was produced, which on repeated manipulation became tetanic. There was slight stiffness of the neck and complete aphasia. His temperature was up to 103°. Leukocytosis, 12,000.

The convulsions ceased, then started in again. They were controlled by the administration of bromides with the stomach tube. There was a strong probability of this being a case of poli-encephalitis, poliomyelitis of the encephalitic type, first described by Strümpell, with the identical symptoms, especially in consideration of the etiological factor. Careful subsequent examinations, however, showed a very distinct scar on the penis, the contours of the pupils were unequal (anechoria syphilitica), the Wassermann reaction was strongly positive. The spinal fluid showed an excess of lymphocytes, and the Nagouchi reaction was positive. After recovering from the coma, the patient gave a complete history of syphilitic infection. The patient is still at the Hospital, convalescent, and improving daily.

From the sketch of the histories given above, it becomes apparent that the diagnosis of this disease in the acute stage is, to say the least difficult, and under certain circumstances impossible. Some experienced observers state, that the four cardinal symptoms presented are, subjective pain, hyperesthesia, profuse perspiration, and leukopenia. Each one or all of these symptoms may be absent or present. Leukopenia, which is mentioned as a constant symptom is by no means always present. Moderate leukocytosis may be found due to the accompanying catarrhal affection of the respiratory tract or intestinal canal. As the early stages of measles and the great majority of the cases of typhoid fever also show leukopenia, the symptoms is only of value, if it occurs at all, in connection with the whole clinical picture. If the above-mentioned symptoms fail or are inconstant, how then is it possible to obtain the *first clue* to the existence of this disease and to differentiate it from other febrile conditions? I strongly suspect that this is impossible in certain elementary or transitory attacks of a mild character. In most cases, however, we will be rewarded by a most painstaking search for symptoms pointing to an irritation of the cerebrospinal system. It is unnecessary here, to go into a detailed analysis of the well-known signs of the presence and absence, exaggeration and diminution, and variability of the reflexes of the eyes and the muscular system which belongs to a complete neurological examination. The variations exhibited in the reflexes is due in great part to the location and to the irritative or destructive nature of the inflammatory process in the neurones. Recent

pathological study has furthermore shown, that it is not only the meninges, the anterior horns of the cord, the cortex of the brain, and the central nuclei which may be affected, but also the posterior horns, in fact, any part of the brain and cord may be implicated. The variability of the nervous symptoms is in itself if not characteristic, very suggestive. The taking of a complete nerve status at each visit will soon uncover the mutability of the reflexes, the motor and sensory disturbances. The first point to be looked to is, therefore, to discover, if possible, any sign of meningeal or cerebrospinal irritation. John Lovett Morse¹⁰ has recently corroborated the observations of Brudzinski, who first pointed out two distinct phenomena which are not present in healthy children, or in diseases other than those of the brain and cord. These are: (1) The contralateral reflexes of the legs, and (2) the neck sign. The contralateral reflex consists in the concomitant reflex of the leg on one side, when passive flexion of the leg on the other side is made. There are some variations of this sign. Brudzinski's neck sign is present in meningitis when passive flexion of the neck forward causes flexion of the legs at the hips and knees, and a marked flexion of the legs on the pelvis. Various writers have attached great importance to these signs in the diagnosis of meningitis. Further study must show, whether these reflexes are present in the meningeal forms of poliomyelitis. In a former paper¹¹ I dwelt upon the importance of spinal puncture in the diagnosis and treatment of various diseases in young children. At that time I hardly suspected the significance of the procedure in the diagnosis of the subject now under discussion; although it will take a far more extended experience than we now possess, and perhaps the devising of new methods of investigation to differentiate specifically the spinal fluid found in the various infections. In a careful analysis of over 500 specimens Lucas¹² tabulates the findings—macro- and microscopic of the spinal fluids of the various infections of the brain and cord in young children.

The cases under consideration may be divided into two large groups: (1) Cases with a predominance of polynuclears; (2) cases with a predominance of mononuclears or lymphocytes. The first group includes cerebrospinal meningitis as well as influenzal, pneumococcus, and streptococcus meningitis. In addition to this the characteristic organism is found in the spinal fluid in each instance. The second group, with predominance of lymphocytes, includes meningism, encephalitis, syphilis of the central nervous system, tubercular meningitis, and poliomyelitis. There is no reference to spinal puncture in tetany in the literature.

Let us attempt to differentiate the diseases belonging to the

¹⁰ *Archiv. Pediatrics*, 1910, xxvii, No. 8, 561.

¹¹ *AMER. JOUR. MED. SCI.*, 1910, cxxxix, 542.

¹² *Amer. Jour. Diseases of Children*, March, 1911, p. 230.

group with lymphocytosis in the spinal fluid. In syphilis of the central nervous system, which is comparatively rare in children, the spinal fluid may give the Wassermann reaction. It also gives the positive Noguchi butyric-acid test. In tuberculous meningitis the Noguchi reaction is negative; the tubercle bacillus is present in nearly 100 per cent. of the cases in the spinal fluid, as was shown by Hemenway. As far as encephalitis is concerned, a number of these cases may be of a parasymphilitic nature and give the Wassermann reaction, or they belong to the cerebral or encephalitic forms of poliomyelitis. It is not unlikely that some cases cannot at present be classified.

The subject of meningism¹³ presents serious difficulties and needs further study. The cases belonging to this group must be considered in connection with the underlying infection; the cytology and bacterial findings will vary according to the early or late stage of the disease.

As to poliomyelitis, Flexner and Lewis,¹⁴ Gay and Lucas,¹⁵ and others, have studied the spinal fluid in monkeys and in young children. The result of these studies can best be illustrated by the precise diagnosis of an obscure case from the microscopic examination of the spinal fluid. This was the case of Dr. Frissell: The patient was a young adult in whom all the reflexes were exaggerated, the Kernig sign and Babinski reflex negative, and the neck a trifle stiff. The Widal, and blood culture for the *Bacillus typhosus* were negative. Leukocytes, 12,000. Physical examination was negative. On the fourth day of the disease, the first lumbar puncture was made. Flexner reported that the fluid was turbid, the sediment consisted of a small number of large lymphocytes, a considerable number of small lymphocytes, and very few polynuclears, and that the clear supernatant fluid gave the Noguchi reaction. The condition of the fluid resembled that seen in inoculated monkeys, just before the onset of the paralysis. On the fifth day of the disease, the reflexes nearly disappeared and there were indications of paralysis of the lower limbs and abdomen. A second spinal puncture showed that the fluid was clear and still contained an excess of lymphocytes. The Noguchi reaction was not so strong. This second fluid resembled that of monkeys after paralysis had set in. The diagnosis and prognosis of this case were made by the most advanced clinical and laboratory investigations.

Nothing is more commendable in clinical medicine than to lay special emphasis upon the thorough observation of the case in hand in all its various clinical aspects. All our methods of observation, both at the bedside and in the laboratory, should be brought to bear on the determination of the given case, just as in criminal

¹³ Johns Hopkins Hosp. Rep., 1904, xii, 379, and Richard Stein, *Ibid*.

¹⁴ Archives of Pediatrics, 1910, xxvii, No. 2, p. 93.

¹⁵ Archiv. of Int. Med., 1910, exxix, 542.

law the jury sifts the evidence of the witnesses and takes note of the impression made by the prisoner. The finger-print method of identification seems at present, however, destined to become the scientific test which will outweigh the sum of all the circumstantial evidence; so in our own field the special diagnosis of disease by laboratory methods is advancing in leaps and bounds. Bacteriological, serological, biochemical tests have opened a great vista in the recognition of disease by scientific methods. In acute poliomyelitis we are dealing with a disease, sudden in onset, short in its course, with symptoms obscure and elusive. Although the attempt to diagnosticate it by the serological method has so far been futile, let us hope that its recognition by a simple scientific laboratory test—not to speak of its prevention, cure, and extermination—will be effected in the not too distant future.

A CLINICAL CONTRIBUTION TO OUR KNOWLEDGE OF POLIOMYELITIS WITH CORTICAL INVOLVEMENT.¹

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It can hardly be supposed that the more intensive study of epidemics of poliomyelitis of recent years accounts for the bizarre clinical manifestations of this disorder which are now of frequent report. The situation would seem of more rational explanation on the ground that the isolated atypical forms of the disease were overlooked or disregarded in the past. The bulbar and pontine types are now common and well defined, but the cerebral and especially cortical involvements are still subjects of debate despite the classic and well-known contentions of Strümpell and his school on the subject.

The existence of a true encephalitic type of poliomyelitis is difficult to differentiate clinically as well as pathologically. In the first place, a spastic palsy is not definite proof of cortical or encephalitic involvement, and secondly, when the autopsy has shown cortical or meningeal alteration the findings have been susceptible of explanation upon other causative grounds. It is not sufficient to state that an encephalitic type must show a cortical lesion and present evidences of notable meningeal irritation, resulting in hemiplegia, which later becomes spastic, but the character, onset, and clinical course of such cases must be a matter

¹ Read before the New York Neurological Society, October 3, 1911.

of careful inquiry before a diagnosis of cortical involvement is possible. Opponents of Strümpell's views no doubt hold too rigidly to a true clinical picture of poliomyelitis itself to admit of many of the bizarre symptoms which must obtrude themselves into the make-up of the clinical syndrome of the cerebral type of the disease. A mere report of a sequential palsy, flaccid or spastic, is susceptible of varied interpretations in the individual case. Many times the apparently associated spastic-flaccid states reported are but instances of flaccid palsy with contractures in normal groups of muscles. Taking the matter by and large, there can be no doubt that the few and infrequent case reports of Strümpell's type show that polio-encephalitis in its typical form is seldom encountered in epidemics of acute poliomyelitis and perhaps occurs only in certain epidemics. Thus, in the Report of the Collective Investigation Committee on the New York Epidemic of 1907, on Epidemic Poliomyelitis,² it is stated that "while the committee do not doubt the rare occurrence of the cerebral (cortical) type of the disease, no undoubted case of this form was reported and in not a single family was it stated that one child was affected with the acute spinal form of the disease and another with the acute cerebral form. Strümpell's hypothesis of the analogy between polio-encephalitis and poliomyelitis is still in need of strict clinical and anatomical proof. The cases previously reported by Moebius, Pasteur, Bucelli, and the doubtful ones of Hoffman and Strümpell are the only cases that offer any support to Strümpell's contention."

Even when we consider the less debatable form, the meningeal type, the subject is not less complicated and is equally difficult to demonstrate in the epidemic disease. It is very difficult to exclude the other kinds of meningitis, not alone epidemic cerebro-spinal meningitis but also tubercular meningitis.³ Meningeal irritation in acute poliomyelitis is not necessarily an initial symptom, but may develop after some days of malaise, etc. Epidemic cerebro-spinal meningitis may occur at the same time and place as epidemic poliomyelitis and must, therefore, be excluded. Even a very wide questionnaire study of epidemics by Zappert⁴ failed to establish a complete picture of any meningeal form. He cites 4 cases supplied by this correspondence study. In one family a child, aged eight years, died of meningitis, while one, aged four years, developed a mild case of monoplegia (left leg), and one, aged three years, a paraplegia following what was apparently a severe gastro-enteritis. In another household attack, one child developed a

² Nervous and Mental Disease Monograph Series, 1910, No. 6, p. 53.

³ Koplik, The Cerebral Forms of Poliomyelitis and their Diagnosis from Forms of Meningitis, AMER. JOUR. MED. SCI., June, 1911, No. 471, p. 788.

⁴ Epidemic of Acute Anterior Poliomyelitis, Jahrb. f. Kinderheilkunde, 1910, Band lxxii, S. 107.

paraplegia, its sister a meningitis which ended in recovery. In a third family, two children developed mild transitory meningeal symptoms. Of more interest was a fourth family episode. One child developed meningeal symptoms from which it recovered, but a monoparesis remained (right leg dragged in walking). A brother also developed a meningeal syndrome and temporary right hemiplegia resulted.

While most of us are, therefore, prone to admit, both from clinical as well as pathological evidence, that meningitis may *co-exist* with acute epidemic poliomyelitis in the same subject, an *exclusively* meningeal type appears to be doubtful. If one looks for proof of encephalitis in epidemic poliomyelitis by the presence of cerebral diplegia alone, classic instances of the association are even more rare than the pure meningeal forms just considered. Most writers upon the subject have heretofore confined themselves to this rather rigid test of a pure encephalitic type. If, however, the latitude of inquiry is enlarged to permit of a hemiplegic type also, as well as certain cerebral symptoms known to be cerebral or cortical in origin (such as choreas, athetoses, aphasia, and convulsions), data are not so difficult of attainment. Thus, in the Swedish epidemic of 1905, Wickman saw no cases of spastic hemiplegia, but other symptoms were recorded which pointed to a cerebral localization. Thus, a boy, aged five years, had the usual febrile onset with violent spasms. He could not speak or leave his bed. The spine was somewhat rigid and tender. The head was bent backward, the hands and arms were weak. He was unable to stand without aid. In about a week he had improved greatly, but still dragged the left leg. The knee-jerks were heightened. In this case the motor aphasia certainly showed a cerebral lesion. A medullary location could be excluded. The heightened knee-jerks also spoke for cerebral localization. The usual atrophy of poliomyelitis was absent. The presence of meningeal symptoms suggested a meningo-encephalitis. The lesion must have been trivial, as the patient entirely recovered. Lunggren also saw a patient with motor aphasia in this same epidemic. Bohmann also saw two brothers, one of whom had typical poliomyelitis. The other, aged one year, had a severe right unilateral convulsion followed by paralysis of the whole right side. The child quickly recovered. The case was an unmistakable cerebral and probably a meningo-encephalitic form of epidemic poliomyelitis. However, no author has apparently seen the full development of the typical syndrome of poliomyelitis associated with spastic paralysis, which further illustrates the necessity of broadening the clinical picture if we are to gain records of cortical types of poliomyelitis. In autopsies, however, acute encephalitic and cortical foci in typical epidemic poliomyelitis are of rather frequent report. Redlich found hyperemia of certain cortical vessels and round-celled infil-

tration in the basal ganglion. Wickman has found the same round-celled infiltration in the cortex of both hemispheres. They were numerous and disseminated. The same lesion was also present in the central ganglia. In another case cited by Wickman no infiltration was present, but there were areas of hyperemia and slight transudation with abnormal richness in nuclei. It must be said, however, in nearly all cases the lesions were of microscopic dimensions. In autopsies of adults the coincidence of old poliomyelitic and encephalitic lesions have also been recognized. Clinical data in this connection, while few in number, are of great interest. Flaccid and spastic paralyses have been seen side by side in children of the same family by Mobius, Medin (4 cases), Pasteur, Bucelli, and Hoffmann. In 1899 Williams reported an association of flaccid and spastic paralysis in the same patient. The child was first seen when eleven years old. When only five years she had headache and convulsions followed by right hemiplegia and asphasia. In a little over a year she recovered or at least improved. He found spastic paralysis of the right arm with flexion contracture. This arm was stronger than the left, probably from its constant choreic twitchings. The right leg was smaller than the left. The knee-jerks were normal. Electric reactions for arm and leg muscles were normal save for the peronei, which showed reaction of degeneration. Analogous cases have been reported by Neurath, Calabuse, Negro, Oppenheim, Maric, and Rossi.

Wickman saw an analogous case as far back as 1899. A girl, aged eleven years, showed evidence of an encephalitis in infancy, before she had learned to walk. The legs were weak for a year, but recovered enough so the child could creep about. When the little patient was first seen, at the age of eleven, there was a high degree of paresis of the lower extremities more marked on the left side. She was unable to stand or walk unaided. When assisted to walk the gait was paralytic, not spastic, but flexing one knee brought out resistance. The muscles of legs were atrophic. There was no reaction of degeneration, but the electric reactions were weak. Intelligence was depressed. Left knee-jerk abolished, right increased. Complete analysis of muscular and tendon phenomena points to an association of cerebral and spinal lesions.

One may summarize the cerebral involvement in poliomyelitis on its anatomic-pathological side as follows: There may be a disseminated encephalitis affecting not only the white substance of the pons and crura cerebri, but also the gray matter of the cortex and regions of the central ganglia. The process, in some instances, would seem to originate in the pia, thus furnishing an important document for the fact that in the epidemic disease the palsy or injury may be a cerebral instead of a spinal one. The random and often unilateral character of the lesion in the cortex is a parallel picture to the pure spinal types. The rarity of the cerebral type

is accounted for by Wickman on the ground that epidemic poliomyelitis is an ascending disease and, therefore, must tend to involve the bulb before it reaches the brain. However, it must be said that in experimentally induced poliomyelitis in apes, no encephalitis can be induced, thus seeming to contradict this theory of extension of the virus up the cord by means of the lymph spaces. It is, however, impossible to inoculate the ape's cortex or subdural spaces directly. We are, therefore, forced to conclude that the lumbosacral cord is most predisposed and the cortex least so. As before mentioned, a simple spastic state cannot necessarily be ascribed to a cerebral, or at least, a cortical involvement, as not infrequently the bulb shows such extreme involvement that the pyramidal tract at this juncture is often seriously damaged.

Thus, Müller has seen 4 cases of spastic paralysis none of which could be explained by a polioencephalitis of the cortex solely. One of his cases, a child, aged seventeen months, suddenly developed a spastic hemiparesis after a febrile attack. This was explained by a lesion of the pyramidal tracts within the pons as shown by the crossed peripheral facial palsy. In another case there was a spastic state in one lower extremity and a flaccid palsy in the other. In still a third, there was a hypotonic paresis of the leg and a hypertonic paresis of the arm. There can be little doubt that in the majority of cases with spastic palsies the lesions inducing the same are at the bulbo-spinal level rather than cortical. A very few cases, however, are on record, as reported by Müller and Förster, where a disseminated encephalitis must have been the predominant lesion. I am not aware, however, that any one has reported an exclusive encephalitic lesion in a case of undoubted clinical polioencephalitis. In other words, the clinical and pathological report have not yet coincided in the one case. If the spastic state is, therefore, not a criterion of cortical involvement and can only be considered presumptive evidence, what other facts must we include to make the lesion definitely a clinical as well as a pathological fact? Obviously, the presence of chorea or athetotic movement cannot be a part of the positive criteria as lesions giving rise to these symptoms may be, and indeed are, most frequently subcortical in origin. True motor aphasia, enduring mental enfeeblement such as idiocy and genuine grand mal epilepsy would seem to make the diagnosis of cortical involvement positive. Of all these phenomena genuine and enduring epilepsy might be definitely considered to make the diagnosis of a cortical lesion most certain. I have, therefore, such a case report.

F. S., aged eighteen years. He suffered greatly from indigestion and constipation as a baby. When aged two years, he had one teething convulsion. When aged nine years, after an accidental fall in the water, he had a single convulsion on attempts at resuscitation. When aged fourteen years, he had a typical

attack of poliomyelitis as follows: The day before the paralysis set in he had fever, vomiting, prostration, and a convulsion; the next morning he attempted to walk across the room; he had taken but a few steps when he fell and suffered a complete paralysis of all voluntary muscles. The patient suffered a good deal from pain in the muscles of the lower extremities. He slept poorly, but was not delirious. He remained acutely ill for two or three days, could not sit up for several days and was able to stand only with crutches after two or three weeks. The paralysis improved slowly but steadily from above downward. He used crutches to get about for six months. When I first saw the patient one year ago for his grand mal epilepsy which has occurred regularly two or three times every three or four months since the attack of poliomyelitis, he showed a steppage gait, more marked in the right foot. There was moderate palsy and atrophy in the tibials and peronei of the legs. There were reactions of degeneration and some shortening of both postici. The whole condition was most marked in the right leg. The knee-jerks were barely present, being difficult of attainment on the right. There was a normal big toe reflex.

Here, then, is a case of poliomyelitis and epilepsy associated in the same case. Can it be considered a mere coincidence? It may be urged that the occurrence of a convulsion at dentition would argue against the case being one of epilepsy induced by cortical injury in poliomyelitis at fourteen years of age. When one bears in mind, however, the fewness of eclamptic convulsions in infancy that terminate in epilepsy, not more than 2 per cent., the importance of the attack at dentition is of little moment. Again, the boy having a convulsion the result of asphyxiation at eight or nine, after a prolonged submersion (ten minutes), but shows the predisposition to convulsions upon a sufficient cause presenting itself. The ordinary frequency with which spasm and convulsions are encountered at the outset of all infectious fevers in infancy ought to cause one to expect the same phenomenon more frequently in poliomyelitis, a disease of sudden febrile onset. Even supposing that the epilepsy in our case was but one of this character, the few cases of epilepsy or eclamptic attacks examined at death, the sequel to infective fevers, bear no distinct pathology of the cerebral cortex not seen in the reported cases of cortical involvement in poliomyelitis. I am fully aware that these and other reasons for looking askance on my case will occur to many; but before I had unearthed the specific fever (poliomyelitis) at fourteen years of age I had given my opinion that whatever the febrile movement was or had been caused by, his disease as we now see it was induced at that time and was dependent upon that particular infection. The usual mental stigma of a pure idiopathic epilepsy is not here in evidence. The disease

in its classic form appeared promptly and has endured since the severe attack of poliomyelitis. Indeed, the first grand mal attack with bladder incontinence and tongue biting came on *pari passu* with the fever and prostration of the poliomyelitis at its inception.

It would seem that we have strong evidence that this patient suffered a diffuse cortical injury at the onset of the poliomyelitis, leaving organic changes in the cortex producing his epilepsy. I can find no similar case on record. The epilepsy in my case has responded illy to the usual hygienic plan of treatment so beneficial in pure idiopathics. The case is placed on record at this time as a clinical contribution to the possible occurrence of cortical injury in a case of otherwise classic poliomyelitis. The residue of the cortical involvement is shown in an enduring epilepsy, a fairly well-proved cortical disease.

While it must be admitted that general or focal convulsions do occur at the onset of polioencephalomyelitis these convulsions or phenomena are for the most part epileptiform in character, lacking the complete picture of genuine epileptic fits, or, they are confined to the acute onset of the epidemic disease or, at least, to the very few days immediately following the attack. There are no cases I have been able to review in the literature in which the convulsions continued as genuine epilepsy in after years such as I am here recording. It is, of course, quite conceivable that this outcome might be expected to occur, as in my case, but it has not come to my notice. The above explanation and disposition holds good for such cases as those of Müller, Zappert, D'Alloco, and Brorström.

It is true that no two nervous disorders are mutually exclusive and in the natural order of events one might expect a certain but small number of epileptics who also had suffered a poliomyelitis. I have seen or known of but one such case in an experience covering several thousand examinations. It may be of interest to cite briefly the details of this one case:

L. L., male, aged thirty-eight years, suffered from a mild attack of poliomyelitis when aged eight years, which affected the whole right extremity. There is now a wasting of the whole right leg from the hip downward and some shortening has resulted. Slight talipes equinovarus and contractures in tibialis posticus of this same side is in evidence. Left knee-jerk is nearly absent while the right appears nearly normal. Achilles jerk is active on the left side and absent on the right. There is a normal big toe reflex. Reaction of degeneration is present in tibials and peronei. There was a neurotic family history and alcoholism in the father. Patient's first seizure occurred at eighteen. The attacks were grand mal in type, preceded by no aura and were mostly nocturnal. At first the attacks occurred every two or three months; now they are

of weekly onset. There is considerable mental deterioration at present.

The case was admitted to my service at Craig Colony several years ago and is still there, a confirmed epileptic. I am indebted to Dr. Shanahan, Superintendent of the Colony, for the case notes here given.

NOTE.—Since this article was written, Richard Stern⁵ has published a study upon the future of poliomyelitic children, and has found two cases of epilepsy developing several years after the initial disease. His material embraces 107 cases of poliomyelitis. This author suggests that so long an interval between the poliomyelitis and the subsequent epilepsy took place that suspicion is justified that the affections were coincidental. No data whatever are added. The cases are identical with my case, L. L., in which epilepsy was sequent to poliomyelitis contracted in infancy and in which the comitial disease appeared ten years after the onset of the acute poliomyelitis.

THE VALUE OF NAUHEIM BATHS IN NEPHRITIS WITH HIGH BLOOD PRESSURE.

By E. AVERY NEWTON, M.D.,

BAD NAUHEIM, GERMANY.

DURING 1905 and 1906, while associated with the late Dr. Heineman in his work at Nauheim, I paid particular attention to the blood pressures of patients before, during, and after taking the baths, and found in cases of high blood pressure (170 mm. Hg. and over) resulting from kidney complications, that the warm saline baths had a more beneficial effect than the cooler baths containing carbonic acid gas.

Up until that time I had always shared the general belief that Nauheim baths were absolutely contraindicated in all cases of marked kidney disease, and in the literature on the use of the Nauheim treatment which I have consulted, kidney disease, when mentioned at all, is regarded as a contraindication to the baths.

The first thing mentioned by Heineman¹ under contraindications to the Nauheim treatment is chronic Bright's disease. Richard Greene² says: "After numerous trials, carefully watched and carefully conducted, Schott found that almost any form of heart disease was benefited by the treatment he elaborated. I have said

⁵ Jahrb. f. Psychiatrie, etc., 1911, No. 182.

¹ Medical Record, June 22, 1901.

² The Schott Treatment for Chronic Heart Diseases.

almost, because it would manifestly be unsuitable for thoracic aneurysm, and much care would have to be observed in treating cases of extensive aortic insufficiency. Also in cases complicated by arterial capillary fibrosis, and small granular kidney." While Groedel³ as recently as 1910 expressed the following opinion: "Bei patienten mit ungewöhnlich hohem blutdruck, 190 mm. Hg. und mehr, haben wir zuweilen, gerade infolge der vermindering des blutdruckes, schwindelanfälle gesehen. Meist sind dies patienten mit gleichzeitiger nierenaffektion. Wir warnen deshalb davor, solche patienten zur kur nach Nauheim zu schicken, desgleichen patienten mit sehr grossen aneurysmen."⁴

These observers, whose wide experience with the Nauheim treatment lends weight to their statements, voice the general belief on this subject. I have found that nearly all physicians are of the opinion that patients with marked kidney lesions are unsuited to the Nauheim baths. My own experience, however, is at variance with this view, for not only have I failed to find a case of nephritis that has in any way been harmed by taking the baths at the proper temperature, but on the contrary, all of my cases have improved. We know that cold bathing, generally speaking, is harmful in such cases, and the baths as usually employed in Nauheim at a temperature of from 83° to 90° F. (28° to 32° C.) are comparatively cool baths. This fact may explain, in part at least, why patients with kidney disease have, as a rule, actually been made worse by the taking of such baths.

In my work at Nauheim during the past three years I have observed a number of cases referred for the cure, in whom various grades of nephritis were present. All of these cases, without exception, were improved by the use of the mild, warm, saline baths given at or near 95° F. (35° C.). Many of these cases have arrived with systolic blood pressures ranging from 170 to as high as 230, and in all of them the blood pressure has been reduced and the kidney condition improved, in some cases albumin and casts have entirely disappeared. Some of these patients have returned once, and others twice, and in these cases I have found that the benefits derived from the first cure have been lasting, some of them showing no albumin and casts on their return a year later, while in others the albumin and casts, though present, were found in less amounts than on the first visit, and the blood pressure had remained lower.

The beneficial influence on high blood pressure and albuminuria which I have observed following the use of suitable Nauheim baths is best shown by the following cases:

³ Bad Nauheim, 1910, p. 118.

⁴ With patients who have unusually high blood pressure, 190 mm. Hg. and more, we have noticed occasional dizzy spells on account of the diminution of the blood pressure. Most of these are patients who have kidney trouble at the same time. We, therefore, warn against sending such patients for a cure to Nauheim, also patients with large aneurysms.

CASE I.—M. D., aged thirty-seven years, married twelve years; one child living, aged three years; two miscarriages. Severe headaches since miscarriage in 1904; eclampsia at birth of last child, an eight months' gestation. She was totally blind following this for two months, when she began to see rays of light and could tell light and dark. Her eyes have slowly improved, until she now has 1.5 vision. While looking at an object it usually changes color. Nearly everything looks red, changing to yellow or purple.

When this patient arrived at Nauheim, July 19, 1909, her blood pressure was 160, pulse 100, and she was very nervous. The urine contained a trace of albumin, but no casts. As her time was limited, she was able to take only eighteen warm saline baths. On her departure her blood pressure was 130, pulse 80; she was much less nervous, and her headaches were less severe.

She returned on May 17, 1910, feeling much better than on the previous year. She now had almost none of the high pressure and headaches, unless she overdid. Her eyesight was much improved, but far from normal. The blood pressure on arrival was 145, pulse 80. The urine contained no albumin nor casts. While here she was given twenty-three warm saline baths, to the last six of which mother lye was added. She was then sent to Switzerland to rest four or five weeks. She returned to Nauheim on August 4, and was then given eighteen warm, saline baths, to which, after the sixth bath, mother lye was added.

A note taken June 28, 1910, states: She feels much relaxed from the baths, vision steadily improving; every few days she sees things about her clothes and room which she did not notice before. The improvement in detail and color sight is most marked. In 1909 blue, gray, and lavender were all the same color to her, and usually could not be distinguished from white. While in a jewelry store a little over a week ago she looked at two pieces of jewelry—one lapis-lazuli, the other amethyst, one gold mounted, the other silver. Both looked alike to her then. Two days ago she was looking at them and the colors were quite distinct. She says that her ability to distinguish colors has improved remarkably the last few weeks since she has been taking the cure at Nauheim.

In January of 1911 I saw her in San Francisco. She was able to read, write, and play cards. I went with her to the ophthalmologist, who had made repeated examinations of her eyes since her attack in 1906. He told me that for a year or more before her first visit to Nauheim her eyes had not improved, and that he was much surprised at the marked improvement after her return from there, and that there had been even more improvement since the last cure than there had been after the first course of treatment at Nauheim.

She returned to Nauheim for treatment on July 20, 1911. Her blood pressure was 135, pulse 70. Her urine was free of albumin, and there were no casts. She had had practically no headaches

except very slight ones after indiscretions in diet. While here she was given sixteen thermal or brine baths. The blood pressure and pulse remained the same.

CASE II.—M. L., aged fifty-eight years. He arrived at Nauheim July 27, 1909. He had been first sent to Nauheim in 1901 on account of cardiac dilatation and endocarditis. At that time he was only able to take a few baths, and had to use a wheel chair constantly. A week after he left Nauheim he began to feel much better, and gained constantly. He returned in 1902, took the first and second cure, was much improved, and continued to feel well several years thereafter.

Three years ago, on awakening, he found his right leg cold. When examined by a physician a thrombophlebitis was found. Later he was sent to Nauheim, where examination showed that his heart was dilated, the left border extended one and one-half inches beyond the left midclavicular line; the first sound was weak and diffuse, the second sound normal; his blood pressure was 160, and his pulse 104. He was given sixteen warm saline baths and four thermal, sprudal baths. His blood pressure was gradually reduced to 130, and his pulse came down to 80.

His urine on arrival showed albumin, 0.014 per cent., and hyaline and granular casts. One week later the albumin was 0.012 per cent., there were hyaline, but no granular casts. Ten days later there was 0.003 per cent. of albumin, a very few hyaline, and no granular casts. On August 25, eight days later, the quantity of albumin was too small to estimate quantitatively, and there were no casts.

CASE III.—An attorney, aged fifty-eight years, arrived at Nauheim July 22, 1910. He used tobacco and alcohol moderately; had always slept well until a short time before, and when first seen was sleeping poorly. His appetite was ravenous, bowels very constipated. In the spring of 1897 he had a severe attack of "la grippe," and was much prostrated. During his convalescence he had a relapse, with an attack of acute Bright's disease, which lasted for several weeks. He had no further trouble until the spring of 1910, when he noticed marked shortness of breath on going upstairs or going up an incline. This became progressively worse. He had an attack of heart failure early in May, 1910, after which he was unable to work or exert himself in anyway. He came to Nauheim to avoid petty annoyances, more fancied than real. His son, who accompanied him, had to watch him closely, as most of the time he was confused. Had to break the journey twice between Antwerp and Nauheim because of fatigue.

Examination showed that the heart was enlarged; the left border extended two inches outside of the midclavicular line, the first sound was about normal, but the aortic second was markedly accentuated. The pulse was irregular, and as nearly as could be

estimated had a rate of 92. The blood pressure averaged 180, with occasional beats up to 190. While at Nauheim the patient was given twenty-six warm, termal baths. Improvement was marked in the character of the pulse, and quality of the heart sounds. The heart diminished in size, until on his departure, the left border of cardiac dulness was just outside of the midclavicular line. In this case the blood pressure did not go below 180. The pulse finally became regular and averaged about 70.

The urine examination on arrival showed albumin, 0.031 per cent., hyaline and granular casts; sugar, 0.52 per cent. One week later the albumin was 0.009 per cent., there were a few hyaline and granular casts, but no sugar. One week later the albumin was down to 0.008 per cent., a few hyaline but no granular casts were present, and sugar was still absent. The last examination made on August 25, 1910, showed only 0.006 per cent. of albumin, a very few hyaline casts, and no sugar.

CASE IV.—A banker, aged sixty-nine years, married, arrived in Nauheim August 2, 1909. He had always been well until 1895, when he had a severe attack of appendicitis; made a slow recovery, and came to Europe where he lived for five years. After this he returned to business and felt able to do more work than usual. In 1907 he noticed some indigestion, and later discomfort after eating. He was examined and found to have a high blood pressure. He spent the winter and spring of 1908 in Egypt and Italy, returned to his home in the United States in April, and felt much better. The following summer he came to Nauheim.

Examination at that time showed his heart to be enlarged, the left border extending about one inch outside of midclavicular line; the first sound weak and the second sound accentuated. He had a slight cold and a good deal of soreness in lower part of his chest, probably due to coughing. He had been having slight nose bleeds. His blood pressure was 190, and his pulse 96. On August 6, at 5.30 A.M., he had such a severe nose bleed that I had to pack the nostril. His blood pressure immediately after this hemorrhage was 160. A little later it went up again to 180. While at Nauheim he was given 25 warm, termal, or brine baths. The blood pressure was gradually reduced to 160.

On his arrival the urine showed a trace of albumin, hyaline and granular casts. The second examination, August 11, 1909, showed a slight increase in albumin, but no granular casts. From this time on, until his departure, albumin and casts were gradually reduced, neither being present when he left Nauheim on September 10, 1909. The heart diminished in size until the left border extended only to the midclavicular line.

I saw this patient again in the spring of 1910. He was feeling decidedly better. There was a very faint trace of albumin in the urine, but no casts were found. He was taking iodide of potassium

on his arrival, and this was continued throughout the treatment, but no other medicines were given.

CASE V.—M. B., aged sixty years. For some years he had been having attacks of dizziness and headaches. He had typhoid fever in 1895, and a bad attack of gout in 1903. A marked eczema had existed for the last twenty years. He used alcohol to excess.

On his arrival in Nauheim, April 28, 1910, the blood pressure was 230 and the pulse 100. While here the patient was given thirty-six thermal or plain brine baths. The blood pressure was gradually reduced, until on departure it was 175, with a pulse of 76 to 80. I have had several letters from this patient during the last winter, and he tells me that he has had no fainting attacks and his headaches are not as frequent or severe as formerly.

The urine examination on arrival showed albumin 0.003 per cent., and a few hyaline casts. One month later the urine showed neither albumin nor casts.

CASE VI.—Female, aged sixty years, arrived in Nauheim June 17, 1909. She had always been well except for headaches and neuritis. Three years ago her left arm became very painful and she was unable to move it. This lasted for six months, then gradually began to improve, and since then she has had practically no trouble in this arm. In April, 1908, she had a similar but less severe attack in the right arm, which began to swell and pained her constantly. I treated her in the winter of 1908 and 1909 in America, by baking, etc., and the arm improved. She remained well after that except for an attack of tonsillitis. She was a poor sleeper, had attacks of indigestion, and her bowels were constipated. Repeated examinations made during my treatment of her in America showed faint traces of albumin in the urine.

Her blood pressure on arrival at Nauheim was 128, and her pulse was 72. Her urine still showed a faint trace of albumin. While in Nauheim she was given twenty-two warm, saline baths. After two weeks the urine showed no albumin, she slept well, and was much less nervous.

CASE VII.—Male, aged fifty-three years, arrived in Nauheim May 5, 1909. He used alcohol and tobacco to excess. He had typhoid fever twenty years ago; double pneumonia ten years ago; four years ago he had a light attack of rheumatic fever which kept him in bed for two weeks. For many years he had had attacks of "intercostal rheumatism," and was subject to frequent attacks of bronchitis. For more than a year the patient had been able to sleep only two or three hours a night. In the latter part of March, 1909, while sitting in a chair after dinner, he fell to the floor, was dazed for about a half hour, could not speak, but knew what was going on about him.

After he reached Nauheim a physical examination showed the following: The breathing was short and jerky. The heart was

dilated, the left border extended one inch outside of the midclavicular line, and the right border the same distance to the right of the right edge of the sternum. The first sound was weak, the second aortic accentuated. The blood pressure was 140, and the pulse 96. His doctor sent with him to me six urine examinations that had been made between December 3, 1908, and February 10, 1909, in all of which a trace of albumin was found.

While at Nauheim the patient was given six plain brine baths and twelve thermal sprudel baths and four sprudel baths. He left Nauheim on June 8, feeling well, but returned on July 11 and took twelve more baths. Examinations of his urine while there showed traces of albumin. His blood pressure was gradually reduced to 115, and the heart dulness diminished until it was about normal.

During the following winter the patient was much more comfortable, and was able to attend to his businesses, which are varied, and require a great deal of mental effort. He returned again in 1910, at which time there was no albumin in his urine, the blood pressure was 115, and the pulse 74. During his third sojourn in Nauheim the patient was given ten thermal baths, ten thermal sprudel baths, and four sprudel baths. During this time there was no albumin found in his urine, nor had there been any up to April, 1911, when I last heard from him regarding his urinary condition. He was feeling well, so well in fact that he did not deem it necessary to return to Nauheim last year. He was able to attend to his duties, had had none of the former fainting attacks, nor the shallow breathing. A member of his family recently told me that the patient was looking exceptionally well, and that his immediate family noticed much improvement in him.

CASE VIII.—A manufacturer, aged forty-nine years, married. He had always been well except that he was nervous from overwork and could not sleep. On November 1, 1908, he was thrown from an automobile, received a severe blow on the head and fractured two ribs; he was able to be up and about in two weeks. While travelling, on December 2, 1908, he had a slight stroke, was conscious, but unable to speak. By the end of that month he was able to walk with the aid of a stick. In January, 1909, he was able to go out for drives, and on January 21 was able to go to the seashore, where he remained until early in May, coming to Nauheim in August of that year.

Examination showed that his heart was enlarged, the left border extending about one and one-half inches outside of the midclavicular line; the sounds were apparently normal; his blood pressure was 210, and his pulse 80. While at Nauheim he was given twenty-three warm, thermal, or brine baths. The blood pressure was gradually lowered, until it was 162, and his pulse was 64, and the left border of his heart extended to just outside the midclavicular line. On arrival his urine showed albumin and hyaline casts. The cast

disappeared after two weeks, the albumin persisted until the last examination made on September 1, 1909, when neither albumin nor casts were present.

When I saw this patient in January, 1910, he was feeling fairly well. At that time his urine still showed neither albumin nor casts.

The patient returned to Nauheim from America in August, 1910. On landing in Hamburg he had an attack of dizziness, which lasted for a minute or two. He was nervous over this, went to a hospital and rested for a week. On his arrival at Nauheim examination showed that the left border of his heart extended to about the midclavicular line. His blood pressure was 170, and his pulse 68. He was given twenty-six warm, termal baths, to which mother lye was added after the eighth bath. His blood pressure fell to 160, and his pulse averaged 66. On arrival his urine again showed a faint trace of albumin, but no casts. Two weeks later the albumin had entirely disappeared.

CASE IX.—Male, aged fifty-seven years. He had typhoid fever in 1868, and pneumonia in 1902. For thirty years he had been treated for stomach trouble. For the last few years he had had difficulty from "gas pressing on the heart," always relieved by belching, and frequent dizzy attacks, especially in a crowded house, theatre, etc. He had pain in the precordial area, and had been taking nitroglycerin from four to six times a day for two years.

On his arrival at Nauheim, June 17, 1910, I found the blood pressure 170, pulse 70, and very irregular, and the heart enlarged to the left as far as the midclavicular line. The patient was given twenty-eight warm, saline baths, with the result that there was a gradual reduction of blood pressure to 152. Although he took no nitroglycerin during the last two weeks of his stay, he had no pain. I saw the patient in New York early in April, 1911, and he told me that he had not taken nitroglycerin during the entire winter, and had had no pain whatever. I found his blood pressure to be 150 at that time.

Urine examination on his arrival at Nauheim showed 0.006 per cent. of albumin, but no casts. Four weeks later there was a very faint trace of albumin present, and a few hyaline casts were found.

CASE X.—Civil engineer, aged sixty-two years, arrived at Nauheim May 19, 1909. For the sixteen years previous to this he had worked in an office. His stomach had been troubling him for two or three years, and he slept poorly. He had a good deal of headache; his bowels were obstinately constipated, and he was extremely nervous.

Examination showed that the patient was very thin and emaciated; there was marked arteriosclerosis; a small amount of cardiac hypertrophy, and his blood pressure was 180 and his pulse 80. While at Nauheim he was given twenty termal or plain brine baths, and three termal sprudel baths; between meals and at bedtime he

drank one and one-half to two glasses of milk, treated with lactic acid bacilli. His blood pressure was gradually reduced to 155 and his pulse to 70.

I saw this patient about six months after his treatment. He had gained fifteen pounds in weight, and was feeling better in every way. He was able to again attend to his work, and had no headaches.

Urine examination on arrival at Nauheim showed a faint trace of albumin, and a few hyaline casts. Five weeks later, at the time of leaving, the urine showed a very faint trace of albumin and no casts.

From the foregoing cases, and many more that I have treated, in which a probable nephritis was present, I am fully convinced that the Nauheim waters, when used as termal or plain brine baths at about 95° F. (35° C.), are beneficial in cases of Bright's disease, and that in treating cases in which albumin and casts are present the waters must be heated to above the normal temperature of the springs, which for Spring No. 7 is 86.2° F. (29.9° C.); and Spring No. 14, 90° F. (32.2° C.). Spring No. 12 is the only one which could be used at its normal temperature, namely, 94° F. (34.4° C.). I have found that the waters, when supercharged with carbonic acid gas as they come from the springs, are not suitable in such cases. Such water would, therefore, have to lie in storage tanks, to be used as termal or brine baths, and in that case would have to be artificially heated, as some of the temperature would be lost while in storage.

Cases I, VII, and VIII are cases that have been at Nauheim for more than one treatment, and showed a definite improvement in the kidney conditions each time they returned. Their condition at the end of the second year, and in one case the third year, was as good or better than at the end of the first year's treatment. The improvement in these cases seems to be of a permanent character.

Cases II and III are cases which showed a marked improvement while taking the cure—Case II especially, in whom the albumin was reduced from a large amount to a faint trace, and the casts, which were present in large numbers on his arrival, entirely disappeared. Case III had 0.52 per cent. of sugar on the first examination made. While under treatment there were three other examinations made, and in none of these later examinations was any sugar found. I do not know whether sugar had ever been found before, so I am unable to draw any deductions as to this condition.

The blood pressure in all of these and in other cases, was lower after the course of baths. In the cases in which the albumin and casts entirely disappear the reduction in the blood pressure is more marked than in the cases in which the albumin and casts only partially disappear. This would lead me to suspect that in such

cases the high blood pressure is largely caused by the kidney condition.

TABLE SHOWING THE BENEFICIAL EFFECTS OF HOT NAUHEIM BATHS ON ALBUMINURIA AND HIGH BLOOD PRESSURE.

	Date.	Sex.	Age.	C.c. of urine in 24 hrs.	Sp. gr.	Per-cent. of albumin.	Casts.	Blood pressure.	Pulse.
Case I	June 20, 1909	Female	37	1500	1014	0.003	0	160	102
	July 30, 1909			1650	1015.5	Trace	0	152	86
	Aug. 12, 1909			1500	1025.	0	0	130	74
	May 22, 1910	38		1200	1018.	0	0	145	90
	June 6, 1910			1400	1018.5	0	0	140	84
	Aug. 23, 1910			2000	1014.5	0	0	130	74
	July 21, 1911	39		1500	1025.	0	0	135	76
	Aug. 3, 1911			1800	1021.	0	0	130	70
Case II	July 28, 1909	Male	58	1500	1019.	0.014	H. and G., few	160	104
	Aug. 6, 1909			1650	1015.	0.012	H., few	130	80
	Aug. 17, 1909			1650	1013.	0.003	H., very few	130	80
	Aug. 25, 1909			1600	1014.	Trace	0	130	82
Case III	July 23, 1910	Male	58	1900	1019.	0.031	H., many	190	92
	Aug. 1, 1910			1400	1018.	0.009	G., few	180	72
	Aug. 9, 1910			1800	1014.	0.008	H., few	180	68
	Aug. 25, 1910			1950	1010.	0.006	H., very few	180	72
Case IV	Aug. 3, 1909	Male	69	2150	1021.	Trace	H., few	190	96
	Aug. 7, 1909			1050+?	1021.5	0.006	G., few	160	80
	Aug. 21, 1909			1950	1021.	Trace	H., few	165	80
	Aug. 26, 1909			1500	1020.	Trace	H., very few	180	80
	Sept. 10, 1909			1530	1024.	0	0	180	80
Case V	May 6, 1910	Male	60	1800	1014.	0.003	H., few	230	100
	June 6, 1910			1950	1008.5	0	0	175	78
Case VI	June 18, 1909	Female	60	1700	1015.5	Trace	0	128	72
	July 4, 1909			1800	1015.5	0	0	130	72
Case VII	May 20, 1909	Male	53	1000	1023.	Trace	0	140	96
	July 13, 1909			1100	1023.	0	0	130	76
	July 14, 1910		54	1500	1021.5	0	0	115	80
	Aug. 3, 1910			1550	1021.	0	0	108	62
Case VIII	July 4, 1909	Male	49	1500	1024.	Trace	H., few	210	80
	Aug. 7, 1909			1650	1024.	Trace	0	170	76
	Aug. 25, 1909			1750	1021.	Trace	0	185	64
	Sept. 1, 1909		50	1800	1014.5	0	0	165	68
	Aug. 8, 1910			1550	1025.	Trace	0	170	64
	Aug. 13, 1910			1800	1014.	Trace	0	160	66
	Aug. 25, 1910			2150	1009.	0	0	162	64
	Sept. 11, 1910			1900	1014.	0	0	160	64
Case IX	June 19, 1910	Male	57	1650	1017.	0.006	0	170	70
	July 13, 1910			1680	1023.	Trace	H., few	152	68
Case X	May 21, 1909	Male	62	1010	1022.	Trace	H., few	180	80
	June 23, 1909			2150	1013.	Faint trace	0	160	20

Just how these baths affect the kidneys is not at this time thoroughly understood. They do cause a relaxation of the entire muscular tissues, as evidenced by the fact that after taking from four to five baths patients are unable to do more than a small percentage of the walking or other exertion of which they were capable before beginning the baths. The baths also relax the per-

ipheral circulation, and this effect may, and possibly does, extend to all tissues of the body. Nauheim baths also cause marked elimination, especially through the skin and kidneys. I have often seen patients who came to Nauheim with a skin almost as dry as a sheet of parchment, after two, three, or four weeks of bathing have an active skin. Indeed, many of these patients remark that they have not perspired for years, even on exertion, but that now, after taking the cure, they perspire easily. This increased elimination through the skin doubtless is no inconsiderable factor in lessening albuminuria and lowering blood pressure.

REVIEWS

BIOLOGICAL ASPECTS OF HUMAN PROBLEMS. By CHRISTIAN A. HERTER, Professor of Pharmacology, Columbia University; Member of Board of Directors (and Physician to the Hospital) of the Rockefeller Institute. Pp. 344. New York: The Macmillan Company, 1911.

THIS book, edited by Susan Dows Herter, from a connected draft not in final form for publication at the time of Dr. Herter's death, represents the interesting and successful attempt of this well-known investigator in, and benefactor of, scientific medicine to set down, for his children, "his interpretation of biological laws in their bearing on human life, in the hope that they may prove of some service to persons who have faith that an understanding of such laws is frequently a help to intelligent and humane conduct."

The biological conception presented is that "human beings are no exception to the rule that all organized beings are in the process of adaptation to their surroundings;" "that all things living are in a state of seething flux, tending to construction or destruction." These tendencies are governed, as the author demonstrates, by quite definite biological laws, which conscious beings may understand and utilize, in order to bring about an intelligent adaptation of the individual to his group of conditions. This rationalistic conception is naturally opposed to the view that religious teachings are the best guide to conduct, and also to the view that each individual has to work out his own salvation by personal experience.

The argument is presented in four "Books" under the general headings: I. The Animal Body as a Mechanism. II. The Self-preservative Instinct. III. The Sex Instinct. IV. The Fundamental Instincts in Their Relation to Human Development. Under the first heading are presented the mechanistic conception of the human body, the problems of growth, reproduction, and inheritance, and a discussion of consciousness and the will. Book II, in four chapters, discusses the instinct of survival, the defences of the body, self-preservation, and the mental life, death, and immortality. Sex instinct is discussed in three chapters devoted respectively to sex and the individual, sex and social relations, and the male and female mind. Book IV presents arts and religion, education and the future of the race, and the fruits of education.

The treatment of these various phases of the subject is a mingling of scientific accuracy and scientific imagination, tintured by a hopeful idealism of personal and social service which renders the perusal not only pleasing, but stimulating, and suggestive as well of possible concrete social effort. It is shown that the mechanistic view of human life does not lead to the hopeless resignation frequently considered as a necessary outcome of scientific fatalism, but, on the contrary, points the lesson of the great possibilities of developing personality through improved education, the increased opportunities for self-development, friendly surroundings, and mutual social service. In the discussion of "Death and Immortality" the idea is brought out that the cutting off of the prospect of heavenly rewards and hellish punishments "would lead to a greater considerateness in all human relations;" that instead of an obtrusive instinct of self-preservation based on a belief in personal immortality, it would develop a desire for mutual helpfulness, with, if necessary, self-sacrificial efforts, in the behalf, for example, of one's offspring. In the discussion of sex is emphasized the great educational and cultured influence of a higher regard (or affection) between the sexes and of the influence of this on ideals and general conduct of life. The refinement and control of the sex impulse, one of the most significant evidences of advancing civilization, the author associates, apparently in causal relation, with what Western nations regard as an improvement in the status of women. The chapter on "Education and the Future of the Race," with the discussions of the relative importance of "observation, memory, and the welding power of reason" as educational objects, and of education in its relation to the sexually based emotions present much of novelty and much that is of distinct value to parents, educators, and physicians; for that matter, this statement applies to the book as a whole.

The reviewer cannot refrain, though perhaps here he goes out of his way so to do, from an appreciation of Dr. Herter, in connection with this, his last message. The book before us exemplifies his character as a "student of man and of nature," and reminds us of his broad humanity and his devotion to the best ideals of his profession. In his work as physician, neurologist, chemist, and pharmacologist (and in the latter capacity he did much to develop experimental pharmacology in the medical schools of New York City), as a director of the Rockefeller Institute and physician to its hospital, as a consulting expert of the United States Department of Agriculture, as an investigator in his private laboratory, as founder and benefactor of the *Journal of Biological Chemistry*, and, with Mrs. Herter, of lectureships known by his name at the New York University and Johns Hopkins University, he was ever actuated by the ideal of service to American medicine and of the wider recognition of science in medicine. Investigator, bene-

factor, organizer, and advisor in all that pertained to medical service in this country, "a presence to be felt and known," he leaves with us, in the posthumous work here reviewed, ideals of effort and ideals of service, so tinged by a vivid scientific imagination, as to constitute a message destined to profoundly influence the progress of science in the profession he labored so earnestly to aid.

R. M. P.

A HANDBOOK OF PRACTICAL TREATMENT. In three volumes. By 82 Eminent Specialists. Edited by JOHN H. MUSSEY, M.D., Professor of Clinical Medicine, University of Pennsylvania; and A. O. J. KELLY, M.D., late Assistant Professor of Medicine, University of Pennsylvania. Vol. II, pp. 865, 103 illustrations; Vol. III, pp. 1905, 47 illustrations. Philadelphia and London: W. B. Saunders Company, 1912.

IN the September (1911) issue of the AMERICAN JOURNAL OF THE MEDICAL SCIENCES (p. 444) appeared a review of Volume I of this System which is completed in Volumes II and III now before us.

The chief aim of this work is to present, in a reasonably small space, a record of the opinions held and the methods employed, in the treatment of disease, by men of recognized authority. These authorities have been chosen from all branches of medicine—thus medicine, surgery, and the specialties, including dentistry, are represented among the eighty-two contributors. Though contained in the space of three volumes, of about 950 pages each, the work may be considered an encyclopedia of the methods of treatment tested and accepted by scientific and authoritative practitioners engaged in the clinical care of the sick. The work is essentially clinical in character, yet the discussions in most instances, deal sufficiently with laboratory investigations to enable the reader to understand the rationale of the measures recommended.

It would be hypercritical for one to compare, in these volumes, the space devoted to therapeutic considerations. Any thought on treatment demands accurate and thorough diagnostic reasoning, and a work which judiciously correlates these will discourage the therapeutic romancer and so be a distinct influence for good.

It is gratifying to note the absence of long discussion, upon drugs and therapeutic measures whose uses are unknown and unsupported by experiment. One finds but few prescriptions and these are, for the most part, composed of drugs whose physiological action is known.

Not only is the treatment considered, but the characteristics of the various diseases are set forth in a manner unusually thorough for such a work; the practitioner, therefore, in considering his treatment thinks in terms of diagnosis, pathology, and prognosis.

So many false prophets have crept into public recognition by means of irrational, extravagant, or fraudulent claims for methods and cures that the union of the diagnostic and therapeutic reasoning of men of recognized standing in medicine constitutes the most important feature of this system.

Systems written, as they are, by authors of widely divergent style and experience are bound to present many variations in quality. The monograph will always be superior to the chapter written for such a work, yet one cannot deny the usefulness to the practitioner of such systems. For example, typhoid fever in Musser and Kelly's work is thoroughly discussed by the physician, the surgeon, the oculist, and the aurist, all of whom frequently consult in the care of this many-sided disease. A feature of the medical consideration of this disease is the detailed account of the steps in "tubbing" with admirable illustrations. The diet in typhoid is fully and practically dealt with. The use of vaccines and sera in typhoid is thoroughly yet conservatively considered.

Sir Clifford Allbutt writes of the diseases of the cardiovascular system. The chapter on the surgery of the heart, while brief, has perhaps the distinction of being the first upon this subject to appear in a work on treatment.

Tuberculosis is most exhaustively dealt with, being allotted 119 pages in a volume of 815 pages of text. The illustrations of institutions established for and of the apparatus employed in the fight against this disease are numerous and instructive. The writer has done well to set forth, in this comparatively small space, so clearly and thoroughly the enormous amount of work done upon the treatment of tuberculosis. This article demonstrates well the therapeutic triumphs resulting in the coöperation of the different branches of scientific medicine.

In the chapter on pneumonia the writer states that "the designation pneumococcic infection is preferable to croupous or lobar pneumonia" because "the inflammatory lesions in the lung may be the smallest part of the process going on in the body and because the extent of the lung involvement has not much to do with the severity of the illness. . . ." and on pages 271 and 272 is a most admirable exposition of the systemic character of the disease. While we have as yet no definite knowledge of how to attack pneumonia as a blood infection, it is to be regretted that the writer, who so clearly points to the systemic character of this disease, has not made a fuller reference to the work done in serum therapy, even though it were only to state where it has failed. Every year the practitioner realizes more keenly that the pneumococcus is not always the only organism at work in this infection, the *anatomical* diagnosis of which is "pneumonia," as the *anatomical* diagnosis "endocarditis" is often only the expression of a destructive streptococcus invasion. An emphasis of the failure of serum

therapy in the infection which we call pneumonia would go far to demonstrate the inefficiency of the drugs so commonly forced upon these unfortunate victims, and to train our minds to think that in antibodies, whether from the system itself or artificially administered, lies the secret of cure. There is, however, throughout the article an emphatic "hands off" to the meddlesome therapist.

Yellow Fever is the title of an article by the late James Carroll published posthumously. One reads with much interest the note appended to this chapter in which Dr. Juan Guiteras (to whom the article was submitted for revision after Dr. Carroll's death) states that "the disease is dying out; in a few years it will be a paleontologic study" (p. 571).

There is a section devoted to tropical diseases (not including yellow fever, cholera, etc.). It might perhaps have been wiser to omit this section. The diseases under this heading are rather superficially dealt with (except malaria), and on this account the book would hardly be useful to those engaged in the present-day energetic study of these maladies, both in the tropics, and at special laboratories. On the other hand, one would not attempt to treat an isolated case upon the meagre information supplied in this work. The bulk of the volume might with advantage have been reduced by omitting this section.

The first 103 pages of Volume III may be considered a clinical monograph upon dietetics in disease. In these pages are included diabetes, obesity, inanition, scurvy, rickets, osteomalacia, arthritis deformans, and gout. Throughout, only one stereotype prescription appears, and drugs are but rarely mentioned. The one prescription is the time-honored "Tr. Nux and Gentian," which has so long been a substitute for a square meal to the starving out-patient that perhaps it should be included among these dietetic considerations.

The feature of the article on diabetes is the diet tables. These differ from those usually appearing in works on treatment in that they are arranged with the aim of supplying the physician a dietary *for the varying phases* of the disease and the different metabolic needs of each case. It is well to add, however, that the text preceding these tables must be read in order to intelligently apply them.

It is refreshing to see but one page allowed to uric acid diathesis and lithemia, and this is devoted to ruling the term and the theory out of medical consideration.

The same fate falls to chronic articular rheumatism, which is disposed of in three-quarters of a page.

Under diseases of the digestive system the physician and surgeon are almost equally represented, and we find an effort throughout to encourage their coöperation early in the disease without necessarily the purpose of operating. The dentist, in whose field we

have come to recognize the source of some of the most destructive and sometimes fatal general septic infections, contributes an article upon general hygiene of the mouth and disorders of the teeth and gums. Too much emphasis cannot be placed upon the importance of including this subject in a work on general medicine. This article deals with those subtle diseases of the teeth and gums often overlooked by astute consultants and clinicians. The writer might perhaps have insisted upon this fact more forcibly and pointed out some of the joint diseases and other septic manifestations far removed from the real and curable cause.

The treatment of nervous diseases and diseases of the mind will be turned to with much interest. This section, taken with the section on hydrotherapy and mechanotherapy which appeared in the first volume will be found to offer much practical assistance to the general practitioner. I am not competent to speak for the alienist and neurologist.

Lack of space prevents further detailed consideration. The general practitioner, and in many instances the specialist, will find in these three volumes a reliable guide, and future authors of systems on treatment will do well to employ this as a model. The publishers have made attractive volumes, which in spite of their size and number of pages, are surprisingly light, and lie open well at almost any portion of the book.

C. N. B. C.

APPLIED ANATOMY. By GWILYM G. DAVIS, Associate Professor of Applied Anatomy, University of Pennsylvania. With 630 illustrations, mostly from original dissections and many in color by Erwin F. Faber. Philadelphia and London: J. B. Lippincott Co., 1911.

THE object of this work is to show the relation of structure to function, whether it is normal function or function disturbed or impaired by injury or disease. The anatomy of the human body is studied in order that medical and surgical treatment may be intelligently applied, and consequently a book of this character possesses greater value than a mere treatise on anatomy, unless the latter is regarded simply as a storehouse of facts. There is a good deal of exaggeration of the value of a minute knowledge of anatomy to the surgeon, but there is no gainsaying the fact that in certain operations, such as tendon and nerve transplantation, plastic operations on joints, dissections of the neck for tuberculous nodes, hernia operations, and some others, the operator will do better work if his anatomical knowledge is exact.

This book seems to accomplish the task admirably, and includes a variety of anatomical and surgical facts, balanced and associated

so as to make an intelligent, interesting, and stimulating presentation of applied anatomy. There are, of course, omissions and statements to which others might take exception, but such must be unavoidable in the preparation of a work of this size by one writer. The purely anatomical portions seem more satisfactory to the surgeon than do the surgical portions, perhaps to the anatomist the reverse might be true, as it is disappointing, when referring to the applied anatomy of a certain operation or disease, to find the technical steps in the operation discussed briefly and without direct connection to the anatomy of the region. For instance, the extension in cancer of the lip is insufficiently treated, and in excision of the tongue no description is given of the anatomical points involved in removal through the neck; the description of excision of the rectum includes removal by the perineal or sacral routes, but no mention is made of the anatomical points involved in removal through the abdomen or by the so-called combined route, a matter of extreme importance. In the description of hernia the antiquated divisions of congenital inguinal hernia are well discussed, as are the various anatomical layers and structures entering into the formation of the canal and rings, but the relation of the sac to the cord, of the femoral vein to Poupart's ligament, etc., are not clearly given. The author seems at his best in the description of the joints, the chapters upon the shoulder and hip being especially praiseworthy; the abdomen, however, is not nearly so satisfactory.

The illustrations are clear, beautiful in execution, and have the faculty of showing what they are intended to show in the great majority of instances. A few, such as the one showing excision of the thyroid gland (Figure 184) convey no idea which might be useful. The general appearance of the book, its binding and printing, is excellent.

G. P. M.

THE MORTALITY OF ALCOHOL. By EDWARD BUNNELL PHELPS, M.A., F.S.S. Pp. 75. New York: Thrift Publishing Co., 1911.

THIS is a statistical study of the causes of death in the United States by alcohol. The author is well qualified for such work, inasmuch as for over twenty years he has edited one of the leading insurance magazines in this country, and in other ways has maintained his interest in the cause of death. He gives comparative tables in which alcohol may have been the cause of death, either as a primary or secondary factor and compares his results with those of the United Kingdom. He comes to the conclusion that the mortality in which alcohol figures directly, indirectly, or even remotely is about 5 per cent., or about 6 in 100 deaths. This is somewhat lower than the estimate given by others, but, taking into consideration the difficulties which enter into such calculation, it is probably a just estimate. The work is well done, and is an interesting contribution.

T. H. W.

INFECTIONS OF THE HAND. A GUIDE TO THE SURGICAL TREATMENT OF ACUTE AND CHRONIC SUPPURATIVE PROCESSES IN THE FINGERS, HAND, AND FOREARM. By ALLEN B. KANAVAL, M.D., Assistant Professor of Surgery, Northwestern University Medical School, Chicago. Pp. 447, with 133 illustrations. Philadelphia and New York: Lea & Febiger, 1912.

THE author has placed before the profession a work that has been much needed ever since surgery has been in existence. Fully appreciating the serious nature of hand infections, and realizing that in the past the treatment of such infections has been inadequate and often ill-advised, due to lack of anatomical knowledge, he has made a most complete study of the anatomy of the hand. By the use of numerous illustrations the relations of tendons, tendon sheaths, spaces, bursæ, and aponeuroses are shown. X-ray plates of bismuth injected specimens and serially sectioned anatomical specimens, show the shape, size, and weak points, by reason of which infection spreads from one fascial layer to another. The work is the most complete on this subject published today, being practically the only one that furnishes exhaustive anatomical descriptions with especial reference to their surgical application.

The book is useful alike to the general practitioner and the surgeon. The index and general arrangement is such that the diagnosis and treatment of a particular case is easily found and followed.

With such a mass of isolated and different facts all of more or less importance and yet so related as to demand mention together, it has been impossible to obtain a clear, concise, and adequate text, without repetition on the one hand, or too much cross reference on the other. The author has made the latter mistake, and consequently has made difficult reading, interrupted every few lines by a reference, which in its turn again refers the reader to a third place. This condition also exists in the legends under illustrations. The reader is referred to the legend of another illustration for the explanation of the lettering on the cut under observation at the time. In one or two instances the illustration and the text do not agree.

In several places the style is distinctly stiff, halting, and confusing to the extent of ambiguity. Too much space is consumed by introductory classifications and case histories.

With the exception of the few above-mentioned adverse criticisms the work deserves the greatest of credit.

The chapters on diagnosis and treatment are ably written and justly emphasize the fallacy of several of the older treatments. Packing with dry gauze for drainage is most justly and severely criticized. Gutta-percha is rightly given first place as a drain. Free incisions, by the bloodless method, are advocated.

In the postoperative treatment the writer advises hot antiseptic dressings, frequently changed, and partial Bier constriction for the first ten to eighteen hours.

A short clear *resume* is given of the literature on infections of the hand as well as the opinions of numerous surgeons on their methods of treatment.

A work fathered by ideas which give such wonderful results as are claimed by Dr. Kanavel is most certainly indispensable to every surgeon and general practitioner.

After reading these results, we better appreciate how little we knew of the surgery of the hand, and what poor results we obtained.

E. L. E.

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO. Vol. I, No. 1, February 1, 1912. Pp. 133; 8 illustrations. Philadelphia and London: W. B. Saunders Company, 1912.

DR. MURPHY is recognized as one of the foremost teachers of surgery in this country; he is also an original thinker, and, what is more, has the faculty of setting his audience thinking. The series of volumes to be published bi-monthly, of which the first is now before us for review, is announced as a *verbatim* report, by an expert medical stenographer, of the remarks made by Dr. Murphy while operating, together with his discussion of such matters as are raised by the operation or the patient's disease.

The range of subject matter is wide, embracing surgery of mammary carcinoma, gastric ulcer, peripheral nerves, pleura and lung, joints, pelvic tumors, hemangioma, fistula in ano, etc. To the spectators of the operations under discussion his remarks during their performance no doubt conveyed some idea of what was being done. To others, who have not seen the operations discussed, no clear idea of the technique of the operation as applied to the individual case is afforded by interjections, exclamations, and ejaculations such as any surgeon utters after he has plunged *in medias res*. If anyone likes gibberish let him read the account of the operations called nerve anastomosis, commencing at page 25. The ulnar and median nerves are as hopelessly tangled in description as they seem to have been in cicatricial tissue, and we have been unable to come to any conclusion as to what really was the nature of the operation employed. "*Valde desirans, Pater optime, vires deficiunt.*" But the clinical lessons which Dr. Murphy derives from the abundant surgical material at his command, when stripped of too frequent pseudoscientific jargon, are clearly and intelligibly enunciated, and are of much value to the larger audience which these volumes will reach.

Might it not be well, in addition to the services of an expert medical stenographer, for the publishers to employ those of an expert medical proof-reader? Dr. Murphy evidently has had nothing to do with the "making" of the book, nor is he to have, so far as can be gathered from the publishers' announcements; and he will be quite as much surprised as anyone to see recurrent references to Henle, when Handley evidently is intended, to learn that in opening the abdomen the rectus fibers were misplaced, instead of displaced, etc.

A. P. C. A.

OUTLINES OF PSYCHIATRY. By WILLIAM A. WHITE, M.D., Supt. Government Hospital for the Insane; Professor of Nervous and Mental Diseases, Georgetown University, Washington, D. C. Second edition; pp. 232. New York: Journal of Nervous and Mental Disease Publishing Co.

THIS is the second edition of White's *Outlines of Psychiatry*. It differs from the first in the fact that the whole subject of paronia has been rewritten and minor changes made. It is an excellent work of its kind for students and physicians who are not specialists in mental disease.

T. H. W.

PRACTICAL CYSTOSCOPY AND THE DIAGNOSIS OF SURGICAL DISEASES OF THE KIDNEYS AND URINARY BLADDER. By PAUL M. PILCHER, A.M., M.D., Consulting Surgeon to the Eastern Long Island Hospital; Late Surgeon to the German, Seney, and Samaritan Hospitals of Brooklyn, New York. 233 illustrations, 29 of them being in colors. Philadelphia and London: W. B. Saunders Company, 1911.

THE introductory chapter deals with the indications for the use of the cystoscope. The first part is devoted to a discussion of cystoscopic technique, including the description of various European and American cystoscopes with their advantages and disadvantages, the care of instruments, and detailed instructions concerning the procedures of a cystoscopic examination. The author describes the appearances presented by a normal bladder, together with the technique of ureteral catheterization with both the direct and indirect cystoscopes. Fifty-nine pages are devoted to the discussion of diseases of the bladder as seen through the cystoscope, and the text is liberally illustrated with pictures of varying merit. Of the numerous functional kidney tests, the author prefers indigo-carmin, phenolsulphonaphthalein, and

phloridzin, and he is of the opinion that these are only valuable in connection with the other and older methods of diagnosis, by the aid of ureteral catheterism. Diseases of the kidney are taken up from the standpoints of symptomatology, diagnosis, and indications for treatment, together with the cystoscopic findings commonly observed in each lesion. The therapeutic uses of the cystoscope are admirably summarized in the concluding chapter. Throughout the book bears the stamp of a man who commands a thorough, practical knowledge of his subject, to whom experience has been the guide in presenting the essential and omitting the unnecessary.

F. E. K.

DIE PALPABLEN GEBILDE DES NORMALEN MENSCHLICHEN KÖRPERS UND DEREN METHODISCHE PALPATION. By DR. TOBY COHN. Part 3, pp. 585; 33 illustrations. Berlin: S. Karger, 1911.

THIS is the third division of this work, the previous two being upon methods of palpation of the upper and lower extremities respectively. It is an excellent presentation, for it details the methods of palpation of all the structures of the head and neck, and as such should be of great value to all clinicians.

T. H. W.

ONE HUNDRED SURGICAL PROBLEMS. THE EXPERIENCES OF DAILY PRACTICE DISSECTED AND EXPLAINED. By JAMES G. MUMFORD, M.D., Visiting Surgeon to the Massachusetts General Hospital; Instructor in Surgery, Harvard Medical School, etc. Pp. 354; 12 illustrations. Boston: W. M. Leonard, 1911.

THIS volume, which forms one of the "Case History Series," constitutes, as Mumford notes in his preface, a return to an older method of instruction—that by example instead of by precept. Writers used to collect several "centuries" of cases, each series consisting of one hundred case histories; and these were published in rather indigestible form. To be of any practical value these ponderous folios and quartos, written when Latin still was the universal language of science, had to be accompanied by an almost equally ponderous index; and to consult any series of similar cases in the tomes of Bonetus, Fabricius ab Acquapendente, Morgagni, or other similar worthies, requires a long working day, much of which is spent in studying the indices rather than the text. Dr. Mumford presents his case histories in palatable form, well arranged according to the regions or organs of the body affected, and accompanied with a modest but useful index, as well as a table of diagnoses.

The case histories are interesting, at times entertaining; and always convey important lessons of diagnosis, prognosis, or therapeutics, which are enhanced by the intercalation in the text of epexegetical commentaries and *obiter dicta* quite characteristic of the author. On page eleven, the misprint (?) gastrocolic omentum should, we presume, be changed to transverse mesocolon; for whereas a form of *anterior retrocolic* gastro-enterostomy was in fashion at one time in Germany, it does not seem likely that Dr. Mumford really advocates a *posterior antecolic anastomosis*, which is what is actually described. But when a surgeon drains every simple case of acute appendicitis for forty-eight hours, there is scarcely any intra-abdominal feat which he might be regarded as incapable of performing.

To say that the book is a very good one, is perhaps too faint praise; to say that it is not as good as some other somewhat similar and now classical volumes, such as Billroth's *Clinical Surgery*, for example, is within the truth.

A. P. C. A.

PRACTICAL NURSING. FOR MALE NURSES IN THE R.A.M.C. AND OTHER FORCES. By MAJOR E. M. HASSARD, R.A.M.C., and A. R. HASSARD. London: Oxford University Press.

ALTHOUGH the authors have written this book primarily for the use of male nurses and orderlies, nevertheless a careful perusal of the work would be of advantage to the average practitioner, usually so negligent of the details of intelligent and careful nursing. The book would also make a good text-book for the hospital training school, as it is clearly written, compact, and thorough. The advice given is serviceable and practical; the faults are those of omission rather than of commission.

J. H. M., JR.

PSYCHIATRISCHE VORTRÄGE FÜR AERZTE, ERZIEHER UND ELTERN. By PROF. DR. G. ANTON, Direktion der Klinik für Geistes- und Nervenkrankheiten in Halle, a. S. Pp. 77. Berlin: S. Karger, 1911.

THIS small volume is designed for physicians, educators, and parents, and is of a popular variety. It takes up the question of normal and abnormal development, alcoholism, and epilepsy.

T. H. W.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

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The Relation of Tonsillitis to Milk Supply.—C. E. A. WINSLOW (*Boston Med. and Surg. Jour.*, 1911, clxv, 899). A sudden increase in the cases of acute tonsillitis in certain parts of Boston and its suburbs, was talked of at a medical meeting in Boston on Thursday, May 11, 1911. By Sunday, May 14, there was an increase of 100 per cent. in the cultures examined by the laboratories of the health departments as compared with the previous Sunday. The disease differed clearly from ordinary tonsillitis. The most striking feature was the secondary enlargement of the glands of the neck, which in many cases followed the first sharp throat attack, and which in some instances was followed by a general invasion of the deeper tissues leading to sepsis, rheumatism, erysipelas, nephritis, and other maladies. Its severity increased with age, being usually mild in children. Most of the fatalities occurred in patients over fifty-five years of age. It occurred in a sharply marked epidemic culminating on May 12, 13, and 14. The epidemic, with the single exception of a clinically similar one among school children in Westchester County, New York, in February and March, was confined to Massachusetts. There seems to have been no connection between the two localities. Eighty-five to 90 per cent. of the patients had used milk from the same source, which amounted to less than 1 per cent. of the total Boston supply. Moreover, for the two months preceding the Boston outbreak, the disease was epidemic in the outlying towns around the suspected farm. Presumably a "carrier" infected the milk, producing the epidemic. At the farm itself the cattle are inspected four times a year by a veterinarian, and diseased cows forbidden; the sanitary conditions are regularly examined;

bacterial analyses of the milk are made six times a month; stringent rules are in force against human sickness, and milk from any farm where disease occurs is not used. Yet it cannot be doubted that contamination must, in some way, have occurred. However, against such outbreaks there is one certain safeguard, proper pasteurization with proper protection of milk from secondary contamination. To Winslow's knowledge no milk epidemic of similar throat disease has been hitherto reported in this country. In Great Britain, the phenomenon has been a common one. "Septic sore throat," so-called by the English, must be added to the list of dangers surrounding a raw milk supply.

Disturbances of Respiration Due to Nuclear and Intranuclear Disease.—C. F. HOOVER (*Jour. Amer. Med. Assoc.*, 1911, lvii, 1734) states that the physiology of respiration involves a number of problems; the lung as an aerating organ; the mass movement of the blood; the partial pressure of carbon dioxide and oxygen in the alveolar air and circulating blood; products of metabolism; and finally the nervous control of respiration which may be modified by alterations in the bulbar respiratory centre. He cites loss of consciousness or apnea following morphine in incipient tabes; or the varying effects of that drug in cardiovascular disease with relation to Cheyne-Stokes breathing and slumber apnea. He concludes that the use of respiratory depressants must be employed with great caution when there is any reason for suspecting anatomic degeneration in the respiratory centre. Disturbed respiration also may originate from disturbed peripheral innervation of the lung, due to a neuromuscular reaction with spasm of the bronchioles and deficient lung ventilation, characterized by dyspnea of an emphysematous type, or with tachypnea without cyanosis or impaired lung ventilation. The former is probably due to vagus neuritis, and as an example Hoover mentions a case of mediastinal tuberculosis. The latter is probably due to excitation of the pulmonary branch of the vagus. As examples, Hoover mentions the experiments of Baglioni, who observed that excitation of the pulmonary branch of the vagus produced marked tachypnea and more prompt arrest of the heart with lesser stimulus than when the central end of the vagus was excited. This was born out clinically in Hoover's experience by 2 cases of aneurysm, when the tachypnea was immediately relieved by atropine.

Sahli's Hemoglobinometer.—A. E. BOYCOTT (*Proc. Roy. Soc. Med.*, London, 1911, Path. Sec, p. 43) reports that the two simple hemoglobinometers with a standard composed of hemoglobin or some derivative, are the modifications of the Gowers instrument introduced by Haldane and Sahli respectively. In the former the permanent standard is made by sealing up CO hemoglobin in an atmosphere of coal gas; in the latter it consists of acid hematin. The samples have to be converted before the comparison be made. Though the latter is the simpler instrument, it suffers from material inaccuracies. The standard does not seem adjusted to any definite strength of hemoglobin, normal blood varying from 80 to 120 per cent. with different instruments. In comparing a series of readings with two Gowers-Haldane and Sahli instrument, Boycott observed that, on the whole, the Sahli gave 17

per cent. too low, with the error varying between 8 and 24 per cent. The same sample of oxalated blood from an experimental animal was measured five times in parallel with the two instruments. The largest difference with the first was 5 per cent.; with the Sahli, 22 per cent. Thus Boycott concludes that the Sahli is not an instrument of precision, probably because the pigment is not in solution but in suspension, and because one cannot rely on always making the mixture in precisely the same way. For when blood is mixed with acid, the size of the particles of which the colored precipitate is composed, presumably varies with the precise method of mixture. Hence the depth of tint seen by transmitted light is not always the same, even when the same quantity of the same blood is mixed with the same quantity of dilute acid. (The remarkable variations in Sahli instruments have seemed to the reviewer so great as to render them unsafe for ordinary clinical work.—W. S. T.)

A Characteristic (?) Feature of the Cardiogram.—C. PEZZI (*Compt. Rend. Soc. de Biol.*, Paris, 1911, cxxi, 646) reports that among the numerous signs of adhesive mediastinopericarditis some suggest the presence of concomitant endopericarditis. Pezzi has studied 3 cases in which this condition might legitimately be suspected. In 2 the diagnosis of mediastinopericarditis was confirmed by radioscopy. The cardiogram showed one common feature, lack of any auricular wave. This is explained by assuming that the presystolic wave is due to pressure exerted by the blood driven through the auricle on the apical portion of the ventricle. This, if surrounded by adhesions, becomes non-distendable. Thus no auricular contraction is recorded on the cardiogram. Pezzi considers that this may be an important sign of endopericardial adhesions with apical localization. It must be observed on a number of cases. Finally to be of value, the venous pulse tracing must show an auricular systole. It is this contrast which makes the sign of value.

Compensation by Displacement of the Thoracic Viscera in Pulmonary Tuberculosis.—CHARLES LESTER LEONARD (*Med. Record*, 1912, lxxxi, 1) reports that any alteration in the capacity of the lungs must be compensated for, or the excursion of the walls surrounding must be decreased. Marked alterations in the position of the intrathoracic viscera occur in the earlier stages of tuberculosis without visibly changing the excursion of the thoracic walls, to compensate for the destruction by the disease of the normal expansive tissue. Such can be demonstrated by the stereoröntgenogram. Displacements are of four kinds—displacement of lung by superficial pneumothorax; of heart upward and into anteroposterior position; of heart and aorta to to left or right. The stereoröntgenogram adds to the knowledge obtained by other methods of physical diagnosis by detecting superficial areas of pneumothorax, by showing that the aorta is generally displaced with the heart, and by making evident the effect of fibroid change in displacing the viscera through contraction. Finally, owing to its rapidity, the stereoscopic röntgenogram is more accurate than the fluoroscope, though it does not show the movements of the diaphragm.

Fatty Compounds as a Factor in the Etiology of Appendicitis.—Williams believes that appendiceal concretions are made up of compounds of saturated fatty acids, and that excess in secretion or defect in absorption of calcium and fatty acids may be their origin. A large increase of calcium soaps is found in the submucosa and mucosa of some appendices, in certain cases producing marked thickening. Thus, by cutting off the nutritive supply, bacterial invasion may be made easy. ANTHONY (*Jour. Med. Research.*, 1911, xxv, 359) has studied 48 cases, using various fat stains to differentiate fatty acids and calcium soaps. Her conclusions are that while neutral fats and slight amounts of fatty acids occur in control cases, in acute and chronic appendicitis fatty acids and calcium soaps predominate, and seem to increase with the age of the patient; especially between the ages of twenty-five and fifty years. Thus in general, her observations confirm Williams' views, which are furthered by irregular cultural findings.

The Importance of Estimation of the Urea in the Blood in Bright's Disease.—FERNAND WIDAL (*Bull. et mém. Soc. méd. d. hôp. de Paris*, 1911, 3 s., xxxii, 627). Recent communications have emphasized the importance of the amount of urea in the blood for the prognosis of Bright's disease. Its determination may furnish the only element of certainty obtainable. The normal amount of urea varies between 0.15 to 0.50 grams per liter of blood serum. If more than this, there is nitrogenous retention, which the organism cannot tolerate for any length of time. For example, patients whose blood contains 1 to 2 grams per liter of urea rarely live more than a year; 2 to 3 grams, months or weeks; more than 3 grams, a very short time. In cases of renal obstruction, however, a grave prognosis should not be given, as after the obstacle is once removed the kidney may resume its regular function, and nitrogenous retention cease immediately. In pregnancy an analogous mechanism is assumed by Weill and Wilhelm in regard to nitrogen retention, which they have seen rapidly disappear after delivery. Possibly the same kind of phenomenon occurs in certain acute nephritides in which renal functions may be markedly but temporarily involved. But in chronic Bright's disease retention is more permanent. Certain clinical symptoms suggest nitrogen retention; loss of appetite alone or accompanied by gastro-intestinal troubles; stupidity, often the prelude of terminal coma; finally, of great importance, albuminuric retinitis. But there may be no relation between symptoms and the condition. On the whole, the estimation of the urea in the blood of patients ill with Bright's disease furnishes exact evidence for prognosis, and makes it possible to determine at times a degree of illness which would not be suggested by anything in the patient's general condition.

On the Anti-pneumococcal Powers of the Blood in Pneumonia.—H. E. EGGERS (*Jour. Infect. Dis.*, 1912, x, 48) has undertaken to determine whether or not in cases of lobar pneumonia, an increase of antibodies, and more especially of opsonins, could be demonstrated by the plate method. In a number of cases he preserved serum and leukocytes until an entire series was obtained. Mixtures were then made of pneumonia serum, pneumonia leukocytes, normal serum, and normal

leukocytes, which were incubated on blood agar plates with pneumococci of varying virulence isolated from pneumonia sputum. The amounts used were the same. After varying lengths of time the number of colonies were counted. From his observations, Eggers concludes that in lobar pneumonia there is development of anti-pneumococcal bodies, usually progressing up to the crisis; reaching its maximum at or a little after this time, and lasting for variable periods. That opsonins play a part, at least, in the process is indicated by the fact that the number of plate colonies was in some degree dependent on phagocytosis; that bodies not concerned in phagocytosis, presumably agglutinins, are present is suggested by the fact that the colonies were decidedly fewer in the mixture containing pneumonia serum, than in that containing normal. Finally cases in which the increase of anti-pneumococcal power did not occur, presented irregularities either in course or termination.

SURGERY

UNDER THE CHARGE OF

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The Relations of the Flexures of the Colon to the Kidneys and Kidney Tumors.—HAUSMANN (*Zentralbl. f. Chir.*, 1911, xxxviii, 1657) says that it is a generally recognized fact that kidney tumors are characterized by the demonstrable location of the large intestine in front of them. It is known also that occasionally a tumor not of the kidney may develop between the layers of the mesocolon behind the colon, like a tumor of the kidney. This rule governs tumors of the kidney because the flexures of the colon are adherent to the anterior surfaces of the kidneys, that of the left flexure higher up than the right, the latter being attached over the lower pole. Hausmann has shown that by deep and gliding palpation, the hepatic flexure can be determined to occupy an abnormal position. The sinking of the right flexure is usually, but not always, associated with nephroptosis. If the latter condition is only slight, the flexure can be felt below the kidney. If the nephroptosis is marked, the kidney must first be pushed upward before the flexure becomes palpable. During the ptosis the flexure lies either behind or above the kidney. In 80 autopsies there was no attachment of the right flexure to the kidney in 26, the flexure being always ptosed and movable, sometimes very movable. In these the position of the

flexure was varied and changeable, sometimes above, sometimes in front of, and sometimes behind the kidney. The right flexure can be palpated only when it is attached to the kidney or is only lowered. In the one case it is felt in front of, and in the other below the kidney. When it is behind the kidney, the ascending colon can be followed by palpation upward to the kidney, and the transverse colon from the left to the kidney. When the kidney is pushed upward the covered portion becomes palpable. Tumors of the normally situated kidney lie behind the flexure of the colon. Tumors of a ptosed kidney can lie behind the flexure of the colon, when the flexure has not lost its attachment to the kidney, or it may not have the colon in front of it when the flexure has lost its attachment to the kidney. In the latter case, the tumor lies in front of the colon. Such a relation is less likely in the tumors of the left kidney than in those of the right, because the flexure reaches higher and has a more firm fixation to the kidney on the left side. By gliding movements of the finger tips, deeply sunk, the various portions of the large bowel and stomach are accessible to palpation, and can thus be located. The small intestines are not accessible to palpation, except the end of the ileum before it joins the cecum. Hausmann desires that surgeons as well as internists should avail themselves of this method of diagnosis, and particularly that they should prove at the operation the facts elicited by palpation before the operation.

Thrombosis of the Superior Mesenteric Artery Simulating an Abdominal Tumor.—THÉVENOT and REY (*Arch. gén. d. Chir.*, 1911, v, 1234) report a case of this kind because it presented aspects which differed from those of the typical forms. A man, aged sixty-seven years, was admitted to the hospital, June 12, 1910, for urinary disturbances due to an enlarged prostate. About nine months later he had a suppurative orchitis, and six months later still a perineal abscess which was incised. About a month later, during the dressing of the wound, the patient was suddenly seized with a violent pain in the right flank of the abdomen, and soon developed symptoms of shock. The pain was located below the false ribs, and radiated to the sternum and lower limbs. There was no nausea or vomiting, no stool since the night before, and no tympanities. At the site of greatest pain, a movable mass was palpated, the size of two closed hands, with a notch on its upper surface. It occupied nearly the whole space between the false ribs and the anterior superior iliac spine, and did not move with respiration. Its dulness was continuous with that of the liver. The lumbar region was painful on pressure, and lumbo-abdominal pressure elicited slight ballottement. There was no fluid in the abdomen and nothing was learned by rectal palpation. The temperature was 37°, pulse, 120, and rather feeble. On the following day the peritoneal faeces and the grave general condition continued, and the extremities were cold. The other symptoms were the same, and on the third day the patient died. At autopsy there was found a mass of intestinal loops, violet black in color and distended, corresponding in position to the mass felt in the abdomen before the opening was made. The notch in the mass was formed by a loop of intestine. After separating the coils of intestines, it was found that the lesion was located about 2 meters from the pylorus, the intestine was markedly distended and discolored

for a distance of 50 cm. The adjacent mesentery was profoundly changed. For a breadth of three fingers, it was thickened, indurated, and edematous, of a brownish black color, and the surface was covered with small elevations. On opening the intestine there escaped a considerable quantity of pitchy, blackish liquid. After washing the surface of the mucosa there could be seen ecchymoses, vivid red spots, and some ulcerations, but no perforations. The rest of the intestine was normal. On dissecting the mesenteric vessels, the arteries being largely sclerotic, there was found in one of the branches of the superior mesenteric artery a grayish clot adherent to its walls. On the distal side of the clot the arteries were empty but the veins were engorged with blood. The typical symptoms of an obliteration of the mesenteric arteries are as follows: Early vomiting of the peritoneal type, which is sudden and severe in origin, and may contain blood; intestinal hemorrhages, sometime abundant; diarrhea, especially free at the beginning of the affection, later becoming sanguinolent; general meteorism; and subnormal temperature. The sudden development of a tumor in the abdomen, co-existing with a sudden violent pain is especially significant.

Surgical Treatment of Acute Pancreatitis—KÖRTE (*Ann. Surg.*, 1911, lv, 23) says that the diagnosis of pancreatitis is very uncertain, and can never be made absolutely, owing to our not having as yet found any pathognomonic sign. The signs of peritoneal inflammation are the most prominent feature. When operating for peritonitis, in looking for the point of origin, the pancreas should be considered, and particularly when the inflammation is confined to the upper abdomen. The finding of an odorless, serosanguinous exudate, and even of greater importance, the discovery of small flecks of fat necrosis, is direct evidence of pancreatitis. Early operation is of the greatest importance. Of 16 cases operated on during the first week, 11 recovered, while 5 died. Of 14 operated on in the third and fourth week, one-half died. It is to be hoped that, as with peritonitis, the cases will be sent earlier to the surgeon. As certain results are not to be expected from early operation in this condition as in appendicitis and cholecystitis. The best results were obtained in those cases in which operation was undertaken before irreparable changes had occurred in the gland, in those which did not go on to necrosis, and also in those with encapsulated, inflammatory, hemorrhagic effusions in the neighborhood of the inflamed gland. Good results were also obtained in those cases of localized pus pockets in the pancreas, or in those in which there was a very limited necrosis, as in the acute hemorrhagic inflammations. It is fair to infer that only a small number of cases of acute pancreatitis reach the stage of necrosis, the majority dying before that stage is reached. We must strive to operate before gangrene of larger portions of the gland takes place, to drain the secretion, and where it is possible, to limit the advance of necrosis. This is more difficult in some cases because of the rapid necrosis of the inflamed and hemorrhagic, infiltrated gland. In fact, three or four days after the beginning of the illness it is possible in a few cases to find the gland already advanced in necrosis. The median incision in the early stage is by all means the best, as we can thus reach and treat the diseased organ, and also the gall passages best. The peritoneal exudate should be immediately sponged or washed out with hot saline solution. The pancreas should

in every case be exposed, best through the gastrocolic ligament or from the right side by the liberation and retraction of the duodenum. The approach through the transverse mesocolon is seldom to be advised. The important thing in all operations to consider is that all unnecessary manipulation of the inflamed parts should be minimized, as the danger of collapse is otherwise markedly increased. The exposed organ is, after breaking through the peritoneal covering, incised with a blunt instrument and drained with tubes and gauze strips. The gall passages are also at the same time to be freely exposed for inflammation or empyema. The lumbar incision should be reserved for those particular cases in which there is retroperitoneal collection of pus, and also in the few cases which are operated on in the later stages. Pus in the subphrenic space is best reached through an epigastric incision, and in questionable cases can be sufficiently drained through a transpleural operation. In the stage of abscess formation, hemorrhage from pancreatic and neighboring bloodvessels is a very positive danger, and one which is not entirely obviated through the early operation. Thrombosis of the larger venous channels also occurs, with its consequent septic sequelæ. The pancreatic fistula which develop from the occurrence of tissue necrosis in acute pancreatitis have the tendency to heal spontaneously. The Pawlow-Wohlgemuth diet cure should be employed in each of these cases.

Absorption in Ileus and Peritonitis.—ENDERLEN and HOTZ (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, 755) say that while we are well able to make the clinical diagnosis and construct at the bedside a satisfactory conception of the anatomical picture of the disease, in striking contrast is our lack of knowledge of the cause of the development of the clinical picture, the local anatomical and functional disturbances in the intestine. They undertook to determine by experimentation the nature of the absorption in the small intestine in the various stages of ileus and peritonitis. The experiments were carried out on dogs and in coils of intestine situated at various levels. They tested the absorption of sodium chloride and sugar solutions in different coils, in different concentration, and under varying pressures. In one group of experiments the absorption of the normal intestine was studied, in a second group the absorption in peritonitis, in a third in ileus. A localized peritonitis either does not disturb at all or only in slight degree the absorptive capacity of the intestine involved. On the contrary, we may assume that the local inflammation in consequence of the increased blood supply or inflammatory hyperemia, increases the absorption. This was shown in the experiments by the increased absorption in those dogs in which this function was already depressed. In the early stages of peritonitis the absorption is not decreased. It is first seriously disturbed with the development of general intoxication. In the final stage of peritonitis it is generally much depressed. It can be increased by an excessive secretion. It is believed that the toxic or bacterial general sepsis influences the activity of the intestine by a vasomotor disturbance. In ileus the absorption in the obstructed portion of intestine is much decreased. In all the experiments it was seen that the afferent empty coils of intestine had absorbed a greater quantity of fluid contents than the obstructed segment. This shows that the portion of intestine involved by the ileus has a diminished

absorptive capacity. With the employment of a 5 per cent. saline solution, there was found a marked fluid secretion in the lumen of the intestine. The quantity of this excess of secretion in the ileus coils was twice as large as in the afferent coils, and it was found further that this excess of secretion after seventeen hours was still undiminished. The irritation of the concentrated saline solution has also a much more intensive effect than in the normal intestine. To neutralize the high concentration an enormous quantity of fluid and mucus is produced. The absorptive capacity in the whole intestine, even in that portion not involved in the obstruction is diminished. In a localized peritonitis absorption in the afferent intestine is good, but with the development of general peritonitis absorption in the whole intestine gradually diminishes until stagnation and finally an excess of secretion occurs. There is no question concerning the necessity of early operation in ileus or peritonitis. Unnecessary manipulations within the abdomen are to be avoided. Under certain circumstances one must be satisfied with an enterostomy without seeking to ascertain the nature of the obstruction. The value and effect of the enterostomy is generally recognized. Various factors which damage the intestine are overcome. After the disappearance of the distention there is an inhibition of the irritation and of the disturbances of the blood circulation. Peristalsis and absorption in the intestinal tract are restored, provided that the gut has not reached an advanced stage of paralysis. The exhausted intestine, tired out by the unsuccessful efforts of the increased peristalsis, will not be able to carry off the fecal masses. There will be little necessity of stimulating this by physostigmin, strychnin, and other peristaltic stimulants. Opium should not be administered, but the bowel left to itself.

A Study of Sprain-fracture.—ROSS and STEWART (*Ann. Surg.*, 1911, iv, 71), because of the importance of sprain-fracture as attested by its frequency and location (near joints), made a careful study of this condition from a clinical and experimental point of view. Clinically, the history of sufficient injury with a small, sharply localized area of swelling and acute tenderness over a region of tendinous or ligamentous attachment is diagnostic of sprain-fracture, and should be considered as such whether or not x-ray verifies the diagnosis. Tenderness of lesser degree may surround an acutely tender area. Tenderness lasts, as a rule, from five to twenty days, longer in improperly treated cases; however, those few cases with symptoms as given above, in which tenderness disappears within forty eight-hours, are, nevertheless, sprain-fractures. The acute tenderness referred to is unmistakable; when the spot is firmly pressed on the patient invariably winces. The following conclusions are reached: History of sufficient injury, with a sharply localized area of swelling and acute tenderness over a region of ligamentous or tendinous attachment, means sprain-fracture. X-ray is not essential for the recognition of sprain-fracture. The external malleolus is probably the most frequent seat of sprain-fracture. About 15 per cent. of all fractures are sprain-fractures. That condition, formerly called severe sprain, is sprain-fracture. The condition resulting from stretching of soft parts is better termed strain. Sprain-fracture is probably a part of the pathology of every dislocation. If in doubt as to whether or not sprain-fracture has occurred, treat as a sprain-fracture.

THERAPEUTICS

 UNDER THE CHARGE OF

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The Action of Atophan in Normal and Gouty Subjects.—DEUTSCH (*Münch. med. Woch.*, 1911, lviii, 2652) believes that atophan is by far the best remedy thus far proposed for the treatment of acute gout. It is not surprising that its action is not so marked in chronic gout with marked anatomical changes in the joints. It is also impossible to say as yet whether kidney or heart complications so often associated with gout will be influenced by its use. He summarizes the action of atophan as determined by many different observers, and mentions the different theories advanced for its action. In healthy individuals the administration of small doses of atophan is followed by an increase of the uric acid excretion that is manifest within an hour after the drug has been given. Larger doses of atophan, up to 5 grams, caused an increased uric acid excretion that persists during the following day. The increase in the uric acid ranges from 30 to 300 per cent., and occurs in individuals on a mixed diet and those on a purin-free diet. The purin basis, phosphoric acid, total nitrogen, and total sulphur are not changed, nor is the total amount of the urine increased as a rule. After discontinuing the remedy the uric acid remains at a slightly lower level for one or two days, but soon returns to its former level. With the prolonged administration of atophan the amount of uric acid excreted remains at a higher level when compared to the amount excreted before the drug was given. Similar results are obtained in gouty subjects by the administration of atophan. In addition Frank and Bauch have found that gouty individuals are able to excrete uric acid introduced intravenously, or nucleic acid given by mouth if they receive atophan at the same time. Deutsch gives the details of a number of carefully conducted experiments that in general confirm the above-given facts. He does not draw any definite conclusions from his results. Deutsch used atophan in the treatment of 25 cases of gout with good results. In some of the patients gastro-intestinal symptoms, such as abdominal pain, regurgitation of sour fluid and diarrhea, occurred as a result of the use of atophan. These did not occur when the remedy was combined with sodium bicarbonate.

The Treatment of Intestinal Amebiasis.—MUSGRAVE (*Jour. Amer. Med. Assoc.*, 1912, lviii, 13) says that in acute or chronic amebic dysentery characterized by frequent stools with blood and mucus, and usually accompanied by tenesmus, ipecac given in large doses is a most valuable drug. In the majority of instances its administration is followed by a rapid subsidence of the symptoms, and quick convalescence. In a smaller percentage of such cases it apparently does no

good whatever, and in a not insignificant number its administration is followed by an aggravation of the symptoms which in some grave cases may at least hasten an unfavorable termination, particularly if nausea and vomiting results from the treatment. Musgrave denotes these cases as clinical dysentery, "but besides these typical cases there are many cases without well-defined symptoms, but with etiological and pathological basis for the diagnosis of amebic dysentery. The latter group of patients do not react so well to the ipecac treatment. Musgrave advises giving colon irrigations with patients in the knee-chest position once or twice a day. Two or three liters may be given in this way, and at times patients are able to retain as much as four liters. Thymol, quinine, and silver nitrate solutions are the three that have proved to be of the greatest value. Of these Musgrave prefers thymol and he recommends the following formula because of the insolubility of thymol in water. Thymol, alcohol, āā 25; glycerin, q. s. ad 250. Add 10 c.c. of this solution to each liter of water used in the irrigation. Quinine solution is made up in the strength of 1 to 1000 or 1 to 500 of quinine bisulphate in water. Quinine solutions frequently give rise to constitutional effects produced by its absorption from the bowels, particularly in patients who are able to retain enemas for considerable periods of time. Nitrate of silver, in solutions of from 0.1 to 1 per cent. in distilled water, frequently proves of decided benefit. In his conclusions Musgrave says that each case must be a law unto itself as to the choice of the methods of treatment. The irrigation treatment is the main reliance, particularly in what may be termed average or usual cases. Ipecac is particularly valuable in the presence of clinical dysentery and may be tried either alone or in combination with bowel irrigation. The substance used in enemas should be arbitrarily changed from time to time in cases in which satisfactory progress is not being made by any one method of treatment.

The Combination of Salt-free Diet with Bromide and Iodide Therapy.
 —SURVONAT and CREMIEU (*Rev. de Méd.*, 1911, xxx, 762), in their conclusions, say that a chlorine-free diet is a valuable aid to bromide therapy. This fact is explained by the substitution of bromine for chlorine in the body tissues. They suggest that a similar substitution may take place when iodides are given with a chlorine-free diet. Survonat and Cremieu also warn that toxic symptoms may be produced by small doses of either bromide or iodide when given in this way.

The Treatment of Late Diphtheria Complications with Intraspinal Injections of Antitoxin.—BINGEL (*Deut. Arch. f. klin. Med.*, 1911, civ, 374) says that in the convalescence of diphtheria we are often confronted with grave symptoms that, according to him, are the result of the action of the diphtheria toxin. These symptoms are sudden vomiting, delirium alternating with more or less apathy, and more or less evidence of circulatory failure, such as marked pallor and weakening of the pulse. Treatment must be prompt and energetic to combat this poisoning, and Bingel recommends intraspinal injections of diphtheria antitoxin after withdrawal of a corresponding amount of spinal fluid. The author has been impressed with the lack of benefit

of the ordinary procedures to combat the symptoms of cardiac failure occurring after diphtheria, and reports good results by this method of treatment. He suggests that the intraspinal injection of diphtheria antitoxin be made before the development of these grave symptoms, as a prophylactic measure. When the poison has produced marked changes in the myocardium or brain no benefit can be hoped for from these injections. This treatment relieves promptly when there are no such changes, and shows its value by rapid relief of vomiting and retching, and improvement of the circulation. No untoward effects were observed as a result of the injections, except a slight rise of temperature following the injection. The details are given of 11 cases treated by this method, of whom 8 recovered.

Salvarsan Therapy in Scurvy.—TSUCHINSKY and IWASCHENZOW (*Münch. med. Woch.*, 1911, lviii, 2671) have tested the action of salvarsan in scurvy because of the fact that the mouth symptoms are largely due to infection by mouth spirochetes. Repeated small doses of the drug caused a notable reduction in the number of spirochetes with corresponding improvement of the mouth symptoms. However, they do not attribute any especial curative action of salvarsan upon the disease scurvy.

The Prevention of Fever after Injections of Salvarsan.—WECHSELMANN (*Münch. med. Woch.*, 1911, lvii, 1510) thinks that the rise of temperature and constitutional symptoms following intravenous injections of salvarsan are due to dead bacilli in the distilled water used in making the solution. Consequently he has adopted the method of distilling and sterilizing the water for the saline used in the solution of the salvarsan immediately before the treatment. He says that with this technique he has given more than 150 injections in his office without any fever occurring within four hours after treatment. He considers salvarsan less toxic than mercury.

Vaccine Inoculation, Prophylactic and Curative, of Typhoid Fever.—PHALEN (*Jour. Amer. Med. Assoc.*, 1912, lviii, 9) gives in brief the record of prophylactic typhoid inoculation in the British, German, and American armies. He says that nowhere do we get such convincing evidence for the practice of typhoid immunization as from the records of our own army. Up to the present time over 60,000 men have completed the inoculations, and among this entire number and covering a period of nearly three years, but 12 cases of typhoid have developed, and no death has occurred. The record of the Maneuver Division in camp at San Antonio, Texas, during the last summer has been most instructive. An army division, having an average strength of 12,800 men, all inoculated, occupied the same camp from March to July, and in this command but one case of typhoid developed. This was a mild case in a hospital corps man who had not completed the inoculations necessary for protection. During the same four months there were 49 cases of typhoid in San Antonio, with 19 deaths. Between three and four thousand men were in camp at Galveston during this same period, and in this command no case of typhoid occurred, while the city of Galveston furnished 192 cases of typhoid during the existence of the

camp. The city and the camp had the same water, milk, and food supply, the only difference being that the camp had been protected by inoculation. About 3000 men were scattered along the Mexican border, mostly in small camps, many of them in localities where typhoid was present, yet of this command only one man contracted typhoid, which ended in recovery. Phalen ascribes this practical immunity to typhoid fever entirely to the inoculations. He says that treatment of typhoid fever by inoculations is still in the experimental stage. The fact that the dosage given and recommended by different writers varies between one million and one billion bacilli, shows that this practice is very unsettled. The total number of cases treated by typhoid vaccines is small, but they have been carefully observed by competent observers working with small groups of patients. Phalen thinks that the sum of opinions of these men is unquestionably favorable. Inoculation shortens the fever period, and the total duration of the disease, and it also markedly reduces complications and relapses. Very pronounced amelioration of headache, gastro-intestinal symptoms, and toxemia is usual. All the observers agree that even in the cases in which it causes no improvement it has done no harm. The dosage employed in the earlier cases usually ran from 10,000,000 to 100,000,000. With increasing confidence the dosage has been increasing, and now it is usually from 100,000,000 to 500,000,000. It is probable, according to Phelan, that with increasing dosage, even better results than thus far reported will be obtained. The mortality in all the cases collected from the literature by Phalen was 4.9 per cent., and he believes that the vaccine treatment may reduce typhoid mortality below its heretofore irreducible minimum.

PEDIATRICS

UNDER THE CHARGE OF

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Sodium Benzoate in Artificially-fed Infants.—CLIFFORD GRULEE and WALTER BUHLIG (*Archives of Pediatrics*, 1911, xxviii, 849) determined the general action of sodium benzoate on the bacteria in milk, and studied the effect of the drug in artificial milk mixtures. They used one part of milk as a control, one part contained sodium benzoate 0.1 per cent., and one part contained 1 grain of benzoate to every 6 ounces of milk. The milks were plated every twenty-four hours, and the bacteria counted per cubic centimeter. From these experiments they deduced that with 1 grain of the benzoate to 6 ounces of milk (0.04 per cent.), or in 0.1 per cent. strength, the number of bacteria in milk does not differ materially from the number in control milks; that sodium benzoate in the above strengths has a slight inhibitory effect on some

bacteria; that sodium benzoate is a fair preservative only when few living bacteria are present. The clinical observations consisted in administering sodium benzoate in one-half and one-grain doses in each feeding to infants on artificial mixtures. Some of the infants showed before and during the benzoate administration malnutrition, rickets, gastro-intestinal disorders, and tetany. Grulee and Buhlig give complete histories of 9 cases, including milk formulas, treatment, and results. They conclude from these observations that sodium benzoate to the amount of $2\frac{1}{2}$ to 5 grains in twenty-four hours in artificially fed infants, ranging in age from a few weeks to almost two years, produces no recognizable symptoms, even though these children may be suffering from gastro-intestinal disturbances of a serious nature.

Salt-edema in Older Children.—FRANZ HAMBURGER (*Münch. med. Woch.*, 1912, lviii, 2500) calls attention to the fact that increase or decrease of sodium chloride in the diet has quite an influence on edema. In nephritis or lost cardiac compensation in the adult, edema can be produced and intensified by increasing the sodium chloride in the diet, and then diminished by a reduction of the same. Infants without heart or kidney lesions react similarly, especially where disturbances of nutrition are present. It is possible to accomplish this in older children with normal heart and kidneys. It is essential, however, that some abnormal condition be present to obtain the effects—usually some disturbance of general nutrition. Hamburger cites one case in full, that of a child aged five years, who had suffered a long time from malnutrition and was emaciated. The heart and kidneys were not diseased. Under an increased sodium chloride diet the child gained 3 kilograms in two months, but developed general edema in a marked degree, which disappeared rapidly when salt-free diet was exhibited. The gastric disturbances had disappeared during the process, and the heart and kidneys remained normal. Increase of sodium chloride in the diet will occasionally cause profuse diarrhea, and edema will not develop. Many children with malnutrition or cachexia will react to this test with the appearance of edema. The inference is strong that infants, children, and adults may be constitutionally impaired by ingesting too much salt, and develop edema although the kidneys remain intact.

The Diazo Reaction in Scarlet Fever and Serum Sickness.—S. S. WOODY and JOHN KOLMER (*Archives of Pediatrics*, 1912, xxix, 12) have made a study of the diazo reaction in scarlet fever, diphtheria, and serum sickness to determine its diagnostic value in cases of serum sickness exhibiting a scarlatiniform eruption. A large number of diphtheria cases develop serum sickness with rashes of a scarlatiniform, morbilliform, or urticarial nature. The first type offers the greatest diagnostic difficulty, as it develops from the second to the sixth day after administration of antitoxin. Kerr and Rivier found the diazo reaction invariably absent in scarlatinaform erythema due to serum disease, and the latter found it positive in 56 per cent. of cases of scarlet fever. Woody and Kolmer studied altogether 502 cases as follows: 375 cases of scarlet fever; 56 cases of diphtheria; and 37 cases

of serum sickness. The scarlet fever cases showed the diazo reaction positive in 8.53 per cent. The largest number of positive reactions occurred during the first week of the disease, when the rash was present, and gradually diminished and disappeared with convalescence. Uncomplicated cases of diphtheria showed a general average of 5.4 per cent. positive. Rashes in serum sickness gave a general average of 10.8 per cent. positive. Sixteen cases of the scarlatiniform type showed one positive diazo, or 6.2 per cent. Of 18 urticarial types 2 were positive, or 11.1 per cent. In 3 cases of the morbilliform type none were positive. In the one positive case of the scarlatiniform type, in which there were no other symptoms of scarlet fever, there ensued an uneventful recovery and no desquamation. The positive diazo here may have been due to the diphtheria. Woody and Kolmer place little value on the diazo reaction as a point of differential diagnosis, because it is positive in only 15 per cent. of scarlet fever cases during the first week, and because it was positive in 12.9 per cent. of diphtheria cases during the first week. The reaction was found positive in 75 per cent. of cases of measles. Therefore a negative reaction in a case of morbilliform eruption would be of value in differential diagnosis between serum sickness and measles.

The Hot Air Treatment of Infantile Eczema.—JENNY PERLMANN (*Münch. med. Woch.*, 1912, xlix, 85) reports the results in the treatment of eczema of infants by the application of hot air by means of a cabinet. The results were excellent, not only in the moist forms of the disease, but also in the dry forms, such as the papular, squamous, and vesicular. Most of the cases were infants who had been treated for some months without benefit, by means of the usual salves and ointments. They were considerably under weight, and were in constant distress from itching. After a few treatments the itching and restlessness were markedly improved. During the course of the treatment the children gained in weight, the temperature became regularly normal, and all but the inveterate cases healed in a remarkably short time. It was found that this treatment acted exceptionally well in cases of furunculosis. The furuncles dried up rapidly under the influence of the heat, and soon disappeared, and the further spread of the condition was stopped. A daily application of the hot air was given for from five to ten minutes. The eczematous areas were treated with olive oil between the hot air treatments. Perlmann treated 35 cases in the last six months. The time necessary to cure varied from seven days to three and four weeks. A strict regulation of diet was carried out in each case.

Simultaneous Occurrence of Acute Inflammation of the Heart in Children.—A. FORELL (*Münch. med. Woch.*, 1912, xlix, 142) calls attention to the query of Max Herz, who saw so many identical cases of acute endocarditis at the same time in Vienna, that it suggested to him the appearance of an infectious disease in the form of an epidemic. Forell reports a similar outbreak of acute heart disease in children, in which seven children living in a small area bounded by three city streets were taken acutely ill with identical symptoms. Five of the children were taken ill within a period of forty-eight hours, one child four days

before, and one five days later. They ranged in age from five to ten years. In every case the disease affected acutely and primarily the heart. In no case was there swelling of any of the joints and in but 1 case faint signs of a chorea. The patients comprised two pairs of sisters from two families living close together; one patient lived across the street from them, and the earliest case and the latest case in point of development of the disease lived on the same street as those already mentioned, in adjoining houses. In most of the cases the myocardium alone was involved, in 2 cases the myocardium and endocardium, and in 1 case, in addition to these, the pericardium. One case began with a frank catarrhal angina. In 2 other cases, a history of beginning sore throat was given. The onset in every case was acute, with high fever and marked constitutional prostration, and severe pain over the præcordium. The fever invariably dropped within two or three days, and the temperature remained subnormal for several days. In the myocardial cases arrhythmia and irregularity of the cardiac action developed only after the temperature fell. Only one case, an endocarditis, with myocarditis, showed this symptom before the fever fell, during the second day of the disease. The cases with endocarditis showed involvement of the valves only at the beginning of the second week. Cardiac dilatation occurred in all cases, an increase to the left being always the first sign. In all the cases a true mitral insufficiency existed. Some of the cases showed an enlarged liver and a number had severe nose-bleed. Cultures from the nose and throat in all the cases were negative for the diphtheria bacillus. A blood culture on one case during the febrile stage was negative. The causal factor is problematical. Probability would indicate an acute rheumatic infection from the slight choreic symptoms in one case, the typical rheumatic pericarditis in another, and, finally, the fair recovery of the patients.

The Treatment of Post-diphtheritic Paralysis by Antitoxin.—MAX CROHN (*Münch. med. Woch.*, 1912, lix, 84) reports 3 cases of post-diphtheritic paralysis which responded to subcutaneous injections of diphtheria antitoxin. In all the cases strychnine, digitalis, arsenic, etc., had no effect on the progress of the paralysis. In the first case, a boy, aged twelve years, the paralysis began three weeks after the onset of diphtheria and affected the skeletal muscles in general and the soft palate in particular. Myocarditis and dyspnea developed also, and the paralysis was progressive until 2000 units of diphtheria antitoxin were given subcutaneously. The progress of the condition was halted, and within three days general improvement was marked and recovery was uncomplicated. In the second case a post-diphtheritic paralysis of the legs occurred in a boy, aged four years. One thousand units of antitoxin caused marked improvement within four days. In the third case, post-diphtheritic paralysis occurred in a boy, aged twelve years, four weeks after the onset of the disease. The legs, back, and soft palate were first affected. There was no improvement under arsenic, etc., and in two weeks there was general muscular paralysis with bronchitis, fever, and marked involvement of the soft palate and throat. Three days after the injection of 2000 units of antitoxin the boy was able to drink fluids, and in eight days phonation and swallowing were intact, and there was a marked improvement in the general

muscular weakness. Kohts, who first reported results from this treatment, used large doses of antitoxin, 25,000 to 35,000 units. Crohn achieved as good results with small doses, and observed a prompt and steady amelioration of the condition after one injection. The antitoxin destroys any diphtheritic remnant in the body, whether bacilli or toxin, and makes impossible a continuation of the nerve destruction. There is no necessity for repeating the antitoxin if the first dose causes a halt in the progress of, or a slight improvement in the paralysis. There was no development of serum-sickness in these cases, owing possibly to the smallness, both of the initial and of the subsequent dose of the antitoxin.

OBSTETRICS

UNDER THE CHARGE OF

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Puerperal Mortality.—UNTERBERGER (*Arch. f. Gynäk.*, 1911, Band xev, Heft 1) discusses in a lengthy paper the puerperal mortality in Meeklenberg-Schwerin from 1886 to 1909. In the twenty-four years he finds that 1 in 488 cases of labor terminates in death from puerperal sepsis; 1 in 1480 cases ends in death from tuberculosis; 1 in 1948 cases from death by eclampsia; one in 3454 cases died from embolism; 1 in 3759 from postpartum hemorrhage; 1 in 4291 from hemorrhage complicating placenta prævia; 1 in 8170 from nephritis; 1 in 10,892 from atony and failure of expulsive pains. These statistics are interesting as denoting the relative frequency of the different causes of death in communities where medical matters are under careful supervision.

The Treatment of Hereditary Syphilis.—BAISCH (*Monats. f. Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 3) believes that where clinical signs of syphilis are present in both parents, the indications for the treatment of both are manifest. Where a healthy mother gives birth to a macerated fetus, spirochetes will be found in the adrenals of the fetus and point to infection in the father at some indefinite period. In the Munich clinic, in 190 mothers having such an experience, paternal syphilis was proved in 146. Recent studies show that every mother giving birth to a syphilitic child is infected, no matter how apparently sound she may be. The infection travels by the spirochete through the placenta from mother to child. The possibility of a healthy mother giving birth to a syphilitic child is denied. In all cases, then, treatment must be addressed not only to the father, but to the mother as well. Where syphilitic children are born apparently healthy many show a positive Wassermann reaction. It may be that children are occasionally born of a syphilitic mother who cannot be demonstrated

to be syphilitic. Where the mother becomes infected toward the end of pregnancy the child may not share the infection. It is certainly true that every child born of suspicious parentage must be subjected to modern methods of examination, and if a positive result is obtained, appropriate treatment must be at once begun. Where the reaction is negative the child must be kept under observation and subjected to repeated and minute examinations. The old treatment of syphilis by mercury and potassium iodide was unsatisfactory, so far as the children were concerned, and in many cases after prolonged treatment a syphilitic mother gave birth to a syphilitic child. Salvarsan, in Baiseh's experience, has been given intravenously in doses of 0.4 to 0.6 gram, the average being 0.5 gram. It is more active in its effect upon the spirochete than mercury, and seems to have a better and more rapid result. In 35 cases the Wassermann reaction was always positive, though several injections are needed in old cases to change the reaction. Apparently it is not necessary clinically to secure a positively negative reaction. Should healthy children be born, the treatment must be considered successful. It cannot be denied that occasionally mercurial treatment is successful, although in the majority of cases one cannot depend upon it. In 3 cases treated by salvarsan the results were favorable, so far as the child was concerned. Where salvarsan was injected into the mother Baiseh saw no results upon the child. He believes that it is advantageous to treat the patient during the puerperal period, even though she is apparently well, if she gave birth to a macerated fetus. It is often impossible to give it in one injection, and the opportunity should be utilized in the puerperal state to secure this.

The Treatment of General Septic Peritonitis.—MORISON (*Brit. Med. Jour.*, October 28, 1911) reports among others the case of a multipara in her eighth pregnancy, who introduced a bone crochet needle into her uterus with the object of procuring abortion. The needle broke, and but half of it was recovered by the patient. She walked into the hospital, and immediately after admission had a chill, with a pulse of 120 and a temperature of 106° F. The lower part of the abdomen was tender on pressure, and vaginal examination showed only a three months' pregnant uterus. Operation was done as soon as possible, and the cervix was first divided anteriorly to permit exploration. The needle was found lying across the interior of the uterus, and vaginal hysterectomy was performed. The peritoneum covering the uterus was acutely inflamed, with effusion. The patient recovered. The trend of this paper, and the discussion upon the subject, is to urge prompt operation upon all cases of septic peritonitis. Three depressing factors in these cases require attention: The first is exposure, and it is essential that these patients be kept warm during operation. The second is the danger of prolonged anesthesia, which can be reduced to a minimum by skill on the part of the anesthetizer by reducing the anesthesia to the shortest possible time, and having everything in readiness before the operation is undertaken. In Morison's experience, chloroform was used, in which the laryngeal reflex was deadened, and then ether was substituted. The third and most important factor was the avoidance of rough manipulations of the abdominal

contents. The general principles of drainage were carried out, and in severe cases the patient received about two pints of normal salt solution in a vein, with a small dose of adrenalin at a temperature of 100° F. Proctodysis was employed, and in some patients as much as twenty-two pints was given in twenty-four hours. Lavage of the stomach was useful. The limited use of morphine proved valuable. Purgatives judiciously employed were also useful.

GYNECOLOGY

UNDER THE CHARGE OF

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Vesicocervical Fistula.—KÜSTNER (*Zeit. f. Geb. u. Gyn.*, 1911, lxi, 402) describes an operative method which, he says, in a large series of cases has never failed to cure this condition the first time. He makes a transverse incision in the anterior fornix, and then by blunt dissection, or with the aid of the scissors, completely separates the bladder from the cervix to a point at least 1 cm. above the upper edge of the bladder fistula, believing this to be an essential point in any operation for this condition. A few sutures of fine aluminum-bronze wire are now introduced in such a manner as to close the bladder opening, and to attach it, and a portion of the bladder wall below it, to the intact portion of the surface of the cervix *above* the cervix fistula. The latter is disregarded, or it may be transformed into a fissure by cutting through the bridge of tissue which separates it from the external os, this procedure sometimes being of value in facilitating orientation and application of the sutures. If the vagina is narrowed by scar tissue, or the uterus is very difficult to pull down, much help may be secured by making an extensive Schuchardt incision, or by completely circumcising the portio.

Combination of Tuberculosis and Carcinoma.—Two interesting cases of this condition affecting the female sexual organs have been very carefully studied by v. Franqué (*Zeit. f. Geb. u. Gyn.*, 1911, lxi, 409). One of these was a case of primary carcinoma of both tubes associated with tuberculosis, neither of these processes affecting the uterus or ovaries, except for the presence of carcinomatous metastases on the surface of the latter. In the second case the ovaries were free, both tubes tuberculous only, and the uterine mucosa tuberculous, with carcinomatous areas in the cervix. This patient had been operated on for tuberculous peritonitis several years previously. Franqué thinks that in both these cases the tuberculosis was the etiological factor in the development of the carcinoma, probably the inflammatory infiltration and disintegration of the connective tissue caused by the tuberculosis favoring the epithelial invasion, a condition which has come to be well recognized by most pathologists as occurring in other

organs of the body. It seems probable that in these cases the carcinoma was of multicentric origin, not only in the sense of arising simultaneously in different areas, but also because of arising from both superficial and glandular epithelium. Franqué calls attention to the atypical epithelial proliferation, somewhat suggestive of cancer, frequently seen in connection with tubal tuberculosis; he has found this in his case as well, but does not believe that this is a forerunner of true carcinoma, as the latter appears to him to arise from the unchanged epithelium. He believes that the tuberculous irritation is responsible for both this atypical, benign proliferation, and for the development of carcinoma, and sees in the demonstrated relationship between tuberculous and malignant conditions of the internal sexual organs a further reason for not treating the former conservatively unless operation is specially contraindicated.

End-results of Surgery in Neurasthenia.—REYNOLDS (*Boston Med. and Surg. Jour.*, 1912, clxvi, 275) says that he fully agrees with the conclusions reached at the joint meeting of the American Surgical and Gynecological Societies in 1910 with regard to this subject, namely, (1) that neurasthenia is fundamental in the individual, *i. e.*, that typical neurasthenias occur only in persons who are ill-developed in some particular, (2) that neurasthenia is never *in itself* an indication for surgical treatment, and (3) that it is *not necessarily a contraindication*. He believes that in the past many surgeons have neglected the second proposition, and have performed operations that were never indicated, thereby bringing surgery into much disrepute in this connection, but also that equally grave mistakes have been made by internists and neurologists, who have failed to realize the importance of the third proposition, thereby withholding treatment which might in many instances have been curative. The diagnosis in any given case as to whether the neurasthenia is really due to local lesions, or whether it is of general origin, but is referred by the patient to an etiologically unimportant symptom, is often of the greatest difficulty, but is also of the utmost importance. If after most careful examination it becomes evident that the nervous breakdown has preceded the development of local symptomatology, it will usually be safe to assume that the latter is not the responsible factor; operation should, therefore, be avoided in these cases, even in the presence of a demonstrable but non-lethal lesion. If, however, the local trouble appeared first, and especially if it has persisted unchanged for years, followed by the development of a neurasthenia, the former will generally be found to be the causative condition. A cardinal principle in treating local lesions of a gynecological nature in neurasthenics should be to avoid prolonged minor treatment, for even in cases where this is locally successful, it is almost certain to be generally deleterious. In gynecological work, moreover, radical extirpation of organs is usually accompanied by so much nervous shock as to be equally inadmissible in the treatment of neurasthenic patients; conservative operations should therefore be given the preference in all cases where they are at all possible. By a rational application of conservative surgery of the female reproductive organs in cases where a distinct lesion seemed to be at the bottom of the trouble, Reynolds has been able to cure 82 per

cent. of patients in whom neurasthenia figured prominently in the symptom-complex; he believes, therefore, that if these principles are carefully carried out many supposed *malades imaginaires* will be found susceptible of a prompt cure, or at least of being restored to a fair degree of health and happiness.

DERMATOLOGY

UNDER THE CHARGE OF

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Toxic Dermatoses.—HARTZELL (*Jour. Cutan. Dis.*, March, 1912), in a paper read before the American Dermatological Association, in a symposium on the toxic dermatoses, concludes that such diseases as erythema multiforma, urticaria, dermatitis herpetiformis, pemphigus, and some other bullous affections of uncertain classification, are toxemias due to a great variety of toxic substances which may be introduced into the body from without, may arise from auto-intoxication, or from local or general bacterial infection; and that, although they differ from one another sufficiently in their symptomatology and course to entitle them to be considered as separate and distinct affections, they are essentially one in their pathogenesis. Fordyce (*Ibid*), in a paper on "The Influence of Anaphylaxis in Toxic Dermatoses," read in this same symposium, regards the various forms of disease constituting the so-called erythema group of skin diseases as phenomena of anaphylaxis, and believes that this affords the most plausible explanation of the *modus operandi* of the many causes of these affections.

Syphilitic Erythema Nodosum.—JANSON (*Dermatologische Zeitschrift*, Band xviii, Heft 12) reports a case of secondary syphilis with universal small papular eruption, tendency to hemorrhages, and an erythema nodosum precisely like the idiopathic form of this affection. From the observation of his own case and a study of other cases in literature, Janson concludes that there can be no doubt about the occurrence of a specific luetic erythema nodosum. The treatment of this variety of the disease is that of syphilis, but iodine in combination with other antiluetic remedies seems to be especially effective.

LEVEISEUR (*Jour. Cutan. Dis.*, November, 1911) thinks the resemblance between this form of erythema nodosum and Bazin's disease (erythema induratum) is becoming more and more apparent. He regards it as a malignant form of syphilis (precocious tertiary), which is frequently preceded, accompanied, or followed by gummata.

Telangiectases in Children, in Association with Wasting and Protracted Diarrhea.—FEARNSIDES (*British Journal of Dermatology*, February, 1912) reports a series of 6 cases, all in children, in which telangiectases, erythema, and purpura occurred in connection with wasting and protracted diarrhea. The erythema was present in all the cases and in 5 was associated with telangiectases. Purpura occurred in 2 along with the erythema and telangiectases. The erythema was found usually on the distal portions of the extremities, while the telangiectases were on the thighs and parts of the trunk exposed to pressure. Edema was present in all the cases. Fearnside's concludes that these various rashes were the expression of vascular dilatation, and were the direct result of the wasting brought about by the prolonged diarrhea.

Some Papulosquamous Syphilides and Their Relation to Psoriasis and Parapsoriasis.—RAVOGLI (*Archiv f. Dermatologie und Syphilis*, Band cxi, Heft 1), under the above title, discusses the not infrequent close resemblance existing between some papulosquamous syphilides and psoriasis, and reports briefly some cases in illustration. He concludes that in some instances psoriasis follows syphilis as a metamorphosis of the papular process. In some cases it is a hybrid form to be referred to an attenuated luetic taint; and although not the direct result of syphilis, it can, in many instances, be regarded as a parasymphilitic affection. (We cannot agree with some of Ravogli's conclusions as to the relationship between syphilis and psoriasis. There is no evidence to prove that the two diseases are even remotely related etiologically.—M. B. H.)

The Treatment of Darier's Disease by the Röntgen Ray.—RITTER (*Dermatologische Woch.*, Band liv, No. 6) reports a case of Darier's disease successfully treated by means of the Röntgen ray. In the beginning of the treatment small doses were employed (3 to 5 \times), but without result. Larger doses (10 \times) were then tried, and to these the affection reacted very promptly, the hyperkeratoses disappearing without leaving any scar. Gradually the greater part of the body was exposed to the rays, the result of the treatment being especially brilliant on the face, which was greatly disfigured by hyperkeratoses. The treatment lasted about eighteen months, and Ritter believes the good results permanent.

Eosinophile Cells and "Mastzellen" in Vesicular Eruptions of the Skin.—PULTZ (*Arch. f. Dermatologie u. Syphilis*, Band cxi, Heft 1), who has studied a large number of cases of various vesicular eruptions such as eczema, scabies, herpes, etc., has found a considerable number of eosinophile cells and "mastzellen" in the vesicles of these diseases. In most scabies vesicles and in those of eczema eosinophiles and "mastzellen" were found together, the number of the former, however, greatly exceeding the latter. In the lesions of herpes labialis and progenitalis there was a high-grade eosinophilia and a marked increase in the number of "mastzellen," but in those of 2 cases of herpes zoster neither variety of cell was found. In the lesions produced by vesicants there was likewise a high-grade eosinophile and basophile leukocytosis.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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A Partly Successful Therapy for Cancer.—A preliminary communication of great interest was recently made to the Medical Society of Berlin upon this subject by WASSERMANN, KEYSER, and MICHAEL WASSERMANN. It forms the subject of an article in the *Deutsch. med. Woch.*, December 21, 1911, and of a leader in the *Brit. Med. Jour.*, January 6, 1912. These workers have been seeking a remedy that would exert a selective action upon neoplastic tissues leading to the destruction of those tissues without effect upon the normal body cells, and have met with a partial success in a compound of selenium, tellurium, and eosin. No particulars of its exact qualitative or quantitative nature are to hand, but it may be said that the use of a large dose has led to the dwindling and sometimes to the disappearance of carcinomatous growths in laboratory animals. The growths experimented upon were in some cases transplantation, and in others spontaneous tumors; the curious statement appears that if the required dose be injected into a healthy animal the entire skin of the animal becomes pink (from the eosin), whereas, if a newgrowth be present this does not occur, but the tumor becomes an intense red, indicating a special affinity between the drug and the tumor cells. Tumors as large as a cherry have disappeared under the treatment.

Inflammatory and Arteriosclerotic Kidney Disease.—J. F. GASKELL (*Jour. of Path. and Bact.*, January, 1912), working at Freiburg, contributes a paper containing the results of a painstaking examination of more than 60 kidneys. He concludes that the glomerular and arterial changes give a means of differentiating certain forms of disease that is accurately in keeping with the clinical history of the cases. Among inflammatory cases Gaskell segregates those in which the renal change accompanies ulcerative endocarditis, indicating them as embolic focal nephritides; in these a characteristic fibrinous exudate and leukocytic infiltration affecting some of the glomerular capillaries is found. In such cases, the renal affection is a secondary one and the patient dies from the disease of the heart, and not from uremia, as is likely to happen in the true glomerulotubular cases which are readily separated from the above by the microscopic changes. Permanent inflammatory changes, apart from those seen in ulcerative endocarditis, are always due to true glomerulotubular nephritis, the effects of which are to be seen in different stages, the acute, known generally as acute parenchymatous nephritis, the subacute commonly called "large white kidney," and the sclerotic, usually known as secondary contracted kidney, less well designated "small white kidney." In general, Gaskell

supports the views of Löhlein. The renal changes due to general vascular disease mark an entirely distinct group, which includes those due to senile arteriosclerosis and those in which a true primary contracted kidney, due to arteriosclerosis of the small arteries, are seen. In the former, the senile form, the arteriosclerosis is mainly seen in the aorta and other large vessels, whence it spreads to the renal arterioles, with marked atrophy and glomerular degeneration. Although a high degree of shrinkage may occur, death usually is due to intercurrent disease, and clinically the group is an unimportant one. The latter form, where there is seen a genuine contracted kidney, is seen in cases where a general, well-marked arteriosclerosis of small arteries and arterioles leads to death from such a cause as cerebral hemorrhage.

The Causative Agent of Scarlet Fever.—Much activity has lately prevailed in attempts to convey to monkeys the virus of scarlet fever; prominent among workers have been CANTACUZÈNE, BERNHARDT, VIPOND, LANDSTEINER, LEVADITI and PRASEK. Vipond holds for the causative agent a large, readily-cultivated bacillus. The three authors, last named, inoculated into the tonsils and under the skin, scarlatinal products and produced fairly satisfactorily the signs of the disease, but their animals showed blood cultures of streptococcus; the material does not produce symptoms unless inoculated into the tissues, and one is compelled to think that their experiments allow streptococci to complicate the results, although their own belief is that there are effects that can be attributed only to another virus. More definite, perhaps, are Bernhardt's results with material scraped from the tongues of patients, injected partly under the skin, partly in the mouth-tissues of an ape, of which the inguinal nodes were then emulsified and injected. This was repeated, and the third ape, treated with emulsion that had been filtered through a Berkefeld filter, showed the exanthem, strawberry tongue, fever, subsequent desquamation, especially of the hands and feet, and occasional albuminuria. He thus thinks the disease to be due to a filterable virus, and appends a description of small bodies in the filtrate, which stain readily by Giemsa's method, and which he has found in the nodes and kidneys of individuals dead from the disease.

A Medium for Diphtheria Bacilli.—RANKIN (*Journal of Hygiene*, xi, 1911) has obtained very accurate results in the recognition of diphtheria bacilli by the use of a medium composed of sheep's blood serum, 3 parts; bouillon, 1 part; glucose, 0.5 per cent.; potassium sulphocyanide, 1 part; and 2 per cent. of a 5 per cent. solution of neutral red. The bacillus of diphtheria grows in rose-colored colonies, which are readily distinguished from the colonies of those few other microbes (chiefly cocci), the growth of which is not retarded by the medium.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSON, 1927 Chestnut St., Phila., Pa., U. S. A.

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JOHN HERR MUSSER, M.D., LL.D.

NOT only the medical profession of Philadelphia, but also physicians throughout the United States, as well as his countless friends among medical men of other lands, were shocked by the sudden death of DR. JOHN HERR MUSSER, which occurred in Philadelphia on April 3, 1912, after a brief illness.

Dr. Musser was born in Strasburg, Lancaster County, Pennsylvania, June 22, 1856. It is interesting to note that Dr. Musser was descended from a remarkable line of physicians. Since the

early days of the colony of Pennsylvania, when William Penn granted to one of Dr. Musser's ancestors the right to practise, almost every generation of his family has contributed a representative to the medical profession: his great-grandfather, grandfather, and father all having been physicians of note in their respective communities.

After receiving his preliminary education at the Strasburg High School and Millersville State Normal School, Dr. Musser entered the Medical Department of the University of Pennsylvania, from which institution he received his medical degree in 1877. The following year he spent in the Philadelphia Hospital as a resident physician. Shortly after leaving the hospital he became officially connected with the University of Pennsylvania, which institution he was destined to serve continuously, with extraordinary loyalty and enthusiasm, until the time of his death.

No phase of Dr. Musser's career brought him more pleasure and satisfaction, as well as distinction, than his work as a teacher of medicine. He began as quiz master in the practice of medicine when that form of instruction occupied a well-recognized place in medical teaching. In 1881 he became instructor of clinical medicine in the University of Pennsylvania; eight years later he was appointed assistant professor of clinical medicine, and in 1898 he became professor of clinical medicine in that institution, a position which he filled with distinction until his death. Dr. Musser was essentially a clinical teacher. His keen power of observation, wide knowledge of medicine, and thorough understanding of pathological processes, coupled with a vast clinical experience, rendered him particularly well fitted for bedside instruction, in which he excelled. The thoroughness and painstaking detail with which he studied his patients, together with the energy and enthusiasm which marked his teaching, profoundly impressed his students. Although always alert to be among the first to adopt and advocate every advance in scientific medicine, he was ever mindful of the importance of teaching the art of medicine, and his clinics were replete with helpful and practical suggestions, long remembered by his hearers.

In addition to his activity as a teacher in the University of Pennsylvania, he labored unceasingly in numerous Philadelphia hospitals. In 1884, after serving as a dispensary physician, he became pathologist to the Presbyterian Hospital, and three years later was appointed a physician to that institution, a position

which he held at the time of his death. He served in the hospital of the University of Pennsylvania continuously from 1879, first as medical registrar, a number of years as chief of the medical dispensary, and, finally, as visiting physician. From 1885 he was connected for twenty years with the Philadelphia General Hospital as visiting physician, resigning to become consultant to that institution. Dr. Musser's deep interest in the better development of hospitals in this country claimed his active support in aiding and improving the organization and equipment of the institutions with which he was associated.

From the earliest days of his career until his death, Dr. Musser was a staunch supporter of everything that made for scientific medicine and the betterment of the medical profession. Although a clinician himself, he was keenly alive to the value of experimental medicine, and was virtually the founder of the Department of Research Medicine in the University of Pennsylvania. The Social Service Department now connected with the hospital of that institution owes its successful development largely to his energy and foresight. Always a firm believer in the closer association of physicians with each other, he was a prominent and leading figure not only in the various medical societies of his own city and State, but also in national organizations. The long list of distinguished positions held by him in various societies from time to time, testifies to the high regard in which he was held by the profession, particularly the signal honors which were conferred upon him by his election as president of the American Medical Association in 1904 and his appointment as chairman of the American Committee of the International Medical Congress at Budapest in 1909.

The unflagging energy and extraordinary capacity for work displayed by Dr. Musser are further emphasized by the number and importance of the contributions to medical literature which he found time to publish, notwithstanding the exacting claims of the active practice and multitudinous other interests in which he was engaged. His most notable contribution was his comprehensive work on *Medical Diagnosis*. In addition, he edited, in conjunction with the late Dr. A. O. J. Kelly, *Practical Treatment*, and was an extensive contributor to Keating's *Diseases of Children*, Hare's *System of Practical Therapeutics*, Nothnagel's *System of Medicine*, and Osler's *Modern Medicine*. Moreover, from 1884 until just before his death, Dr. Musser was a frequent

contributor to the various medical journals, and demonstrated his versatility by the ability and authority with which he wrote upon all phases of internal medicine.

Not only was he recognized as a physician of exceptional ability, but he was also greatly esteemed as a broad-minded, public-spirited citizen, eager to aid in every effort for civic betterment, and as a leader in every movement directed toward moral, hygienic, and social uplift. His kindly nature, wholesome optimism, and rugged honesty inspired confidence and affection in all who came under his influence.

Although his untimely death falls most heavily upon the community in which for thirty-five years he labored so untiringly, his loss will be felt by laymen as well as by the medical profession throughout the entire country. Dr. Musser set an example of unselfish, tireless devotion to duty and high professional ideals, supported by unfailing cheerfulness and courage, which can never be forgotten, and which will be a lasting inspiration to all who knew him. To those whose privilege it was to be closely associated with him, his memory will endure as the symbol of all that is best in professional attainment and truest in manhood.

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ORIGINAL ARTICLES

PNEUMONIA.¹

BY J. T. FOTHERINGHAM, M.B.,

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As the seasonal incidence of pneumonia has been distinctly in evidence in our work of the last three or four months, I have selected that familiar, not to say threadbare topic, not in the hope of writing anything particularly new, but in the desire to focus my experience and compare it with that of others in regard to certain phases, particularly of the etiology, clinical course, and prognosis, and especially the treatment.

Space will not permit of any reference to the history of this disease and its literature. "Lung fever" was well known to Hippocrates, and probably earlier, though pleurisy and pneumonia were not distinguished until Laennec, in 1819, described their morbid anatomy, and his work, with that of Auenbrugger, determined the physical signs by which diagnosis is now fairly easy and certain, particularly in the adult. Only so recently as the early eighties was the immediate cause finally determined. Klebs was the pathfinder in the bacteriology of the disease, as in 1877 he described a round motile micrococcus present in the lungs, sputum, and blood. In 1881 Eberth described a similar but different micrococcus, and in 1882 Koch described still another oval-shaped one. In the same year Friedländer detected the microbe named after him, and cultivated and inoculated it, producing a pneumonia which was patchy, but not lobar. Two years later, in 1884, during which time Friedländer's observations were held to be conclusive, Fraenkel

¹ Read at the March meeting of the Médico-Chirurgical Society, Ottawa.
VOL. 143, NO. 5.—MAY, 1912.

and Weichselbaum separated and grew, and successfully inoculated, another microbe, the *Diplococcus pneumoniae*, which has been proved to be much more frequent in pneumonia than Friedländer's microorganism; so that while Friedländer's bacillus is an important microbe of pneumonia, Fraenkel's diplococcus is the recognized cause of the great majority of cases of true lobar pneumonia. It has been clearly shown that the pneumococcus does not necessarily produce only lobar pneumonia, but may cause lobular lesions especially in children; also, that either of these forms of pneumonia may be produced by various organisms, such as the streptococcus, the staphylococcus, the bacilli of putrefaction, anthrax, plague, tubercle, typhoid, influenza, and others. It should be remembered that in pneumonia complicating, for example, typhoid, the lung infection is more apt to be due to the pneumococcus than to the organism causing the original disease. Also, that in some diseases, as influenza; the lung inflammation is apt to be due to the influenza bacillus, if it occur before the height of the illness and to the pneumococcus if the lung complication be a sequel. If it were possible to abandon the useful clinical and anatomical classification of lobar and lobular or bronchopneumonia in favor of the more scientific classification by the germ causing the disease, it might be well, but at present it is neither possible nor, from the point of view of treatment, necessary.

Without following the bacteriology of the disease further, one may define it in two senses—the broad and the narrow. In its broadest sense, acute pneumonia or pneumonitis is any inflammation of the lung, no matter how distributed anatomically, accompanied by acute inflammatory consolidation of the vesicular tissue. In its narrow sense the term is reserved for those consolidations, which form a single mass of considerable extent, generally spoken of as lobar. In the other form, originally designated as bronchopneumonia or lobular, the consolidations are numerous, small, and disseminated, involving, usually, the terminal bronchi primarily, and later their associated vesicles, or groups of vesicles.

INCIDENCE. There is no disease more widespread in all parts of the earth and among all races. It is also one of the most fatal, as well as frequent, of acute diseases. The figures given are: 3 per cent. of all diseases and 6 per cent. of all medical diseases, while the mortality is 6.6 per cent. of all deaths and 12.7 per cent. of all deaths from medical diseases. The average mortality is not less than 1.5 to 2.3 per thousand persons living. I am not, I think, wronging the city of Chicago when I give from memory a statement made years ago that there the deaths annually from pneumonia outnumbered those from tuberculosis. The United States Census of 1900 gave 111,059 deaths from consumption and 105,971 from pneumonia. A few other figures were, in round numbers, as follows: Diarrheas, 47,000; typhoid, 35,000; cholera infantum,

26,000; influenza, 17,000; diphtheria, 16,000; whooping cough, 18,000; septicemia, 7000; scarlet fever, 6000; meningitis, 4000.

Pneumonia of late years seems to be on the increase. American statistics give a rise as follows: Proportion of total mortality, in 1870, 7 per cent.; in 1903, 15 per cent.; in 1904, 19.5 per cent. This must have been due in part at least to influenza epidemics.

Osler states that pneumonia is the most fatal of all acute diseases, killing more than diphtheria, and outranking even consumption as the chief cause of death. Pneumonia remains practically the only infectious process, the incidence and mortality of which is still unaffected by the fact that its etiology is well understood, and by that education of the public in health matters which is producing such excellent results in other infections, such as tuberculosis and typhoid fever. It is perhaps a reproach, and certainly a cause of chagrin to our profession that in spite of a hundred years of general progress, and many and varied methods of treatment for it, the mortality of pneumonia stands unabated.

Its incidence among the urban population is distinctly greater than among the rural. Its seasonal variations correspond closely with those of other respiratory diseases, such as bronchitis and influenza, being greatest during the first four months of the year; although pneumonia, especially as a complication of other conditions, such as typhoid fever or septicemia, may occur at any season.

ETIOLOGY. The influence of season has already been referred to. While all ages are liable, pneumonia is most prevalent, particularly in the acute lobar form, in early middle life. While not infrequent in little children even before two years of age, the patchy type is common, although the statistics for these early ages are somewhat vitiated by the difficulties of diagnosis, and what begins as a lobular may end anatomically as a lobar type of the disease, by coalescence of areas of inflammation. Cases rapidly become more numerous up to the age of thirty years. It should be borne in mind, too, that specific fevers, such as measles, diphtheria, and typhoid are much commoner up to this age, and more frequently accompanied by what is called pneumonia, while influenza has a vastly greater effect than any other specific fever upon the frequency and fatality of pneumonia.

As regards sex, males suffer in the proportion of about two to one female, the difference being explained partly by the greater exposure of males in their occupations, the influence of which must be admitted as a matter of universal experience. Habits, too, of alcoholism and other forms of excess have their bearing, although good authorities state that alcoholism *per se* has no special effect in determining the attack all admit that it enormously increases the fatality, over 60 per cent. of intemperate persons who are attacked dying.

CONTAGION AND INFECTION. The questions of contagion and infection are not yet settled. So-called epidemics of pneumonia are really only local outbreaks due to the same cause in each case, or determined by the incidence of other diseases, particularly influenza. Still, I fancy, none of us has failed to observe on occasions a series of cases arising in the same house, apparently clearly from the first case. Measures of isolation such as are applied to infective diseases have never been hitherto accepted as necessary. More important is the bearing of this question upon the problem of immunity. It is universally admitted that one attack predisposes to another, so that immunity, if conferred at all, is very short-lived, as in diphtheria, where the average period of immunity is fixed at three weeks, so that all efforts at preventive inoculation have so far proved failures. Every successive attack is more dangerous to the sufferer than those that precede. Three, four, and five recurrences are not very rare, and instances of recurrence, even to the twenty-eighth and thirtieth attack have been recorded. Another line of investigation and treatment is that by serums, as in the case of diphtheria. The antitoxin serum as employed first by Klemperer has been actively followed up, but so far without the success for which one might hope. The sera employed have been those of the sheep, the cow, the ass, and the rabbit, as well as that of persons convalescing from pneumonia. There have also been employed the expressed juices of pneumonic tissues, and the filtered and sterilized products of pneumococcus cultures; but the system has not reached what we may call a commercial basis, as in the case of diphtheria, and one is justified in saying that so far the serum treatment has not realized the promise which it at first held out.

Without unduly anticipating as to treatment, it seems fair to say that the vaccine treatment shows more promise of success, particularly in cases of unresolved pneumonia, and in any of the numerous extrapulmonary local infections, such as pleurisy or empyema, pericarditis, endocarditis, peritonitis, otitis, synovitis, meningitis, etc., or in the rare case of generalized infection, the so-called pneumococcus septicemia, particularly where there is no lung lesion.

Many cases reported by competent observers also seem to justify the statement that, as a rule, only an autogenous vaccine is of service, the strains of the organism being so many and varied that stock vaccines are not likely to be of service. A writer in the *British Medical Journal* of June 26, 1909, concludes as follows: (1) Successful inoculation for pneumonia is possible. (2) It does no harm. (3) The vaccine used should be autogenous if possible, if not, it should be from one or more strains known to be virulent. About six days usually suffices to attenuate a virulent strain of pneumococcus. (4) It should be used early. (5) The estimation of the opsonic index is not necessary.

The usual dose is 10,000,000 to 50,000,000 organisms, repeated every two to even ten days, according to clinical indications. I venture to add that vaccines should not entail the nonuse of other approved lines of treatment.

MORBID ANATOMY. It would be a waste of time to go over this familiar ground, but one may note a few outstanding points.

The absence of relation between the size of the lesion and the severity of the constitutional disturbance. One frequently sees a case with a consolidation no larger than a tangerine orange, and very severe fever and other reactions, while another case with double lesions, involving perhaps two-thirds of the lung area, may have much less fever, delirium, and other such disturbances. This may be due to differences in the virulency of the strains concerned, a marked feature of the pneumococcus.

Another very important point in the morbid anatomy is the degree of associated bronchitis. The bearing of this upon such points in treatment as the use of morphine is, as we all know, all-important, and as to prognosis, too much stress cannot be laid upon the fact that bronchitis clearly complicates the outlook, particularly if it has developed in the course of pneumonia. If the pneumonia arises in the course of a preceding bronchitis, or "cold in the chest," the latter is not necessarily so serious a complication. It may be of interest to remind ourselves that the healthy lungs in adults weigh, for the male: right, 24 ounces, left, 21 ounces, total, 45 ounces; for the female: right, 17 ounces, left, 15 ounces, total, 32 ounces. Extraordinary alteration in these weights is observed as a result of pneumonia. Even the sound lung, on account of hyperemia and compensatory change, is heavier than normal, while the consolidated lung has been found, especially the right, to weight over 100 ounces.

With regard to the parts of the lung usually attacked, the order of frequency is (1) the right base; (2) the left base; (3) the right apex; and (4) the left apex, apical pneumonia being relatively much more frequent in children than in adults.

PATHOLOGICAL RESULTS. We may speak of these as death, or resolution more or less complete. In regard to death, it is only comparatively recently that we have realized that death occurs usually not directly because of the condition in the lung, but through the cardiovascular apparatus. Perhaps in some cases the patient may be said to die of exhaustion or asthenia or severe toxemia, the cause of death lying in the higher centres of respiration and circulation; and it may be admitted that other cases die, at least indirectly, because of such complications as tympanites. The latter condition should be looked upon as a complication, in so far as it embarrasses the diaphragm and the heart; but it is even more significant as a symptom of general neuromuscular failure, and is accompanied often by other evidences of the same thing, such as capillary stasis and low muttering delirium.

With regard to the cardiovascular apparatus, the study of the blood pressure has given us valuable information. G. A. Gibson, of Edinburgh, in 1908, in the *Edinburgh Medical Journal*, and G. A. Gordon, in 1910, in the same journal, have shown us that if the blood pressure in millimeters of mercury falls below the pulse rate per minute, recovery is very unlikely. This disturbance of ratio between blood pressure and pulse rate may be looked upon in two ways, and the bearing of the point upon treatment is very important. We have been accustomed, of course, to study this question by watching the first sound of the heart, the second pulmonary and aortic sounds, the pulse, and the degree of dyspnea and cyanosis, and our anxiety rises as these untoward signs advance; but a rapidly rising heart may be due to the attempt to keep full a set of arteries in which blood pressure is rapidly declining. In such cases the use of caffeine, digitalis, strophanthus, strychnine, etc., is urgently called for, while the use of a nitrite would only tend to further handicap Nature's efforts. On the other hand, a heart rate rapidly rising without a fall of blood pressure probably means not a vascular but a cardiac defect, the heart muscle being overpowered by high temperature, toxemia, and particularly by previous disease of the heart, muscular or valvular, which always adds greatly to the patient's danger. In such a case nitrites might be of service if the arterial tension is at such a level as to permit of a lowering that would reduce the burden with which the heart is struggling.

Resolution more or less complete, the other pathological result referred to above, fortunately, is complete in the great majority of cases. Incomplete resolution does undoubtedly occur, for reasons hard to explain; but empyema and all other such results are rarely if ever due to a simple pneumococcus infection. Its greater frequency in children is due to their greater tendency to double infection, and a pneumonia of mixed or doubtful origin is more frequently the cause of empyema in the adult. Such a result as chronic interstitial or indurative pneumonia is perhaps never due to simple pneumonia, but in some cases spreads in from the pleura, following its trabeculæ inward, or begins similarly at the hilum of the lung from chronic inflammation of the glands, interstitial connective tissue growth proceeding after the manner with which we are more familiar in the case of cirrhosis of the liver or of the kidney.

In regard to pulmonary abscess and gangrene, while everyone admits that these conditions may follow on pneumonia, they are always due to secondary infection and probably to a preëxisting one, due to chronic bronchitis, sometimes with bronchiectasis, so that the primary causal connection of pneumonia with these conditions is, in many cases at least, distinctly open to question.

One other point in regard to the clinical course, the pulse-

respiration ratio is of great importance. Normally it is about 4 to 1, 72 pulse beats to 18 respirations. At the outset of the disease, one's suspicion of pneumonia is strongly aroused by observing that this is changed, sometimes even to 2 to 1, pulse rate under 90, breath rate 36 to 40. I need not remind you that dyspnea may be accompanied by either slow or rapid breathing. If obstructive, as in croup or asthma, or from a foreign body in the larynx, the rate is apt to be slow; but I am accustomed to teach my classes that wherever vesicular tissue is affected the breath rate will be quickened, hence the great significance of a breath rate persistently slightly raised, say 22 to 24, in early phthisis. The same holds true much more in regard to pneumonia. Only recently a sthenic case in a young Italian in Ward 6, General Hospital, showed a pulse throughout under 90, with a breath rate up to 40; and more recently still in a profoundly toxic case in Ward 35, General Hospital, whose crisis came only on the thirteenth day, the ratio actually stood once at 88 to 64, or nearly 4 to 3; and though the radial pulse remained good throughout, the first sound of the heart was always faint and poor, a discrepancy of signs for which I had in his case no explanation to offer, as he had no pericardial effusion or other discernible cause for the faintness of the heart sounds, and I cannot think that it could have been due to myocardial degeneration, from the general good conduct of the organ throughout the illness.

I need not say that as a point in prognosis this is most important—not that the mere disturbance in ratio is so important—but that so long as the pulse remains below at most 120, it makes little difference how high the breath rate goes.

PROGNOSIS. Habits and previous state of health: In any given case, habits as regards alcoholism and other excesses may perhaps be mentioned as first in importance as affecting the outlook.

Heart: Perhaps second in importance, if not first, is the state of the heart as to previous disease, muscular or valvular. While many such cases do recover, their danger is immensely greater.

Age: The mortality tables show after five years of age a steadily increasing risk as life advances.

It is of the utmost importance to discriminate between a complicating and a primary pneumonia. Inflammation of the lung arising in the course of influenza, typhoid, apoplexy, or any other disease is much more apt to prove fatal than a pneumonia which is itself the primary disease.

The condition of the non-pneumonic parts of the lung: Where congestion, bronchitis, and edema remain absent from the other parts of the lung the original pneumonic area may become very extensive without seriously jeopardizing life; and the converse is true, that a case with even a small pneumonic area may be fatal if accompanied by extensive irritation in the other areas of the lungs.

We have already referred to the prognostic value of the ratio between pulse rate and blood pressure.

The limitations of general private practice do not ordinarily permit of a white cell count, although we have known for years that a marked increase is of good prognostic significance, while cases in which this fails to occur often die. I am accustomed to teach my classes that where the microscope cannot be used, other almost equally certain evidence of good reaction and good prognosis are as follows: (1) Early and well-defined herpes labialis. This occurs in from 13 to 43 per cent. of cases, according to various authors, and is much more frequently seen with pneumonia than with any other febrile disease. It is sometimes delayed to the fifth or even the seventh day, and if very pronounced and pustular, may be an evidence not of good but of lowered resistance. (2) Sharp and early high temperature, well maintained. (3) The early expectoration of sputum, highly fibrinous, viscid, rusty of course, but not too bloody, and particularly not too fluid, which indicates absence of fibrin and poor reaction. Some at least of these three points, I think, will be found usually to coexist with marked leukocytosis.

Marked neuromuscular relaxation and failure of the nervous system to retain control of the unstriated muscle tissues are signs of gravity. They are shown by the onset of tympanites, of hyper-resonance, and relaxation of other portions of the lungs, and of bronchitis or edema. Especially if associated with low delirium and dry, brown tongue these changes are of serious import.

One may mention finally, not exactly as a curiosity, the loss of the knee-jerk, first referred to in 1894 by that prince of clinicians, Dr. Hughlings Jackson. This reflex disappears usually on the third or fourth day, returns about the ninth day, slightly increased, and becomes normal about the end of the second week in ordinary cases. It has no relation to the crisis, and its disappearance before the third day means danger; while if it remains normal until the seventh day recovery may be considered practically certain. Even in diagnosis this may serve to distinguish tuberculous and other non-pneumococcal pneumonias, in which it usually persists, or is increased.

TREATMENT. I now come to what is after all the most important part of the whole subject, namely, "treatment." Perhaps no disease has been treated in ways so various by what one might almost call differing schools of treatment. Thus we have: (1) What one might call the expectant school, who prefer to wait, leaving everything to nature until she is evidently in difficulty, when some symptom arises which urgently requires relief. (2) Another group is composed of those who believe that early measures are important and who launch out at the outset with very active treatment, believing perhaps that the disease can be aborted or

the oncoming area of consolidation lessened. These two schools stand at the opposite poles of professional opinion. (3) A third group, and one of whom little but bad can be said, might be called "the specific group," who treat every case on the same plan or with the same remedies, ignoring not only the differences in the personal equation of the patient, but the fact that even as a disease pneumonia is subject to very great variations in virulency and therefore in symptoms. (4) A fourth group might be named "the nihilists," who leave everything to nature, as if they believed that any interference was useless or even harmful.

In regard to these groups, one may say that no intelligent physician would nowadays consent to belong to any one of them. About the last group, one may say that it can be only bad policy to make it a rule to do nothing in every case, while it is quite true that many cases do very well with careful watching and practically no treatment.

In regard to the third group, it is almost as unintelligent to have a single plan or a single drug like digitalis, and yet one occasionally hears papers read and discussed at medical meetings by practitioners of this type, of whom it may almost be said in the words of Holy Scripture, "He openeth his mouth and saith unto everyone that he is a fool."

In connection with the second group, it seems to me that there is more reason in their method, particularly if regard be had to the value of such measures as are meant to reduce the toxemia and fever at the outset, such as free purgation, diaphoresis, and diuresis, assuming, of course, that the case is a sthenic one, and seen early.

The views of the opposing schools, if one may call them so, can never be reconciled by appeals to statistics, as it is impossible to obtain a series which differs only in the line of treatment adopted. They differ also in other respects impossible to estimate, such as age, habits, station in life, previous health, season, place in which they live, severity of infection, individual power of reaction, the particular strain of pneumococcus; and the public must trust to the experience, judgment, and common-sense of the physician whom they select.

Let us therefore see what are the main indications in the disease, as well as in each individual case, and this can best be seen by considering how and why death occurs in fatal cases. In most such cases the causes of death are three, namely, toxemia, cardiac failure, or some complication.

A rational treatment, therefore, should have in view the obviating of these three conditions, to which one may add a fourth, the limiting of the lesion in the lung.

TOXEMIA. There seems little doubt that the few cases that were benefited by the old heroic treatment of bleeding at the outset may have been so helped by the lessening of toxemia by abstraction

of blood, which may also have tended to limit the pulmonary lesion mainly by making the blood less fibrinous. But more modern methods of treatment seem to relieve toxemia by free and early catharsis, for which calomel and salines or compound jalap powder are in my judgment best, along with free diuresis. The latter is best obtained by abundant water and perhaps light salines such as citrates, the calomel, of course, acting in the same way. As to diaphoresis, hydrotherapy in the form of hot packs and mustard foot baths are safe and simple methods of securing free skin action, if it be thought necessary.

CARDIAC FAILURE. This can best be prevented only if we clearly understand what is most likely to cause it. Toxemia and fever are the most important causes. Abdominal distention, as everyone knows, is much to be feared for this reason, and the feeding, therefore, should be carefully considered. It seems to me that an excess of carbohydrates and of milk, especially if the patient is rendered flatulent by the salines above mentioned, should be avoided. Constant pain, too, tends to induce cardiac failure, and one of the worst features in the disease is restlessness and delirium. Simple wakefulness is dangerous, and should be controlled by morphine if necessary, but preferably by paraldehyde, 1 to 2 drams, or ammonium or sodium bromide, 40 to 60 grains, both of them administered preferably per rectum. Strychnine should be given before cardiac failure threatens, because in addition to being a good and prolonged cardiac stimulant it is a general tonic. It keeps the respiratory centre awake, and tends to prevent abdominal distention.

In regard to digitalis, while not ignoring the results of laboratory research, rather being grateful for our added knowledge of its pharmacology, this is a case in which one may depend only on clinical evidence as to its value, and it was found to be useful in this disease before its dangers in other acute infections were recognized.

I am accustomed to teach my classes that the use of digitalis presupposes a heart muscle which is histologically sound. Its use is therefore dangerous in such diseases as erysipelas, scarlet fever, septicemia, typhoid, in which usually the patient has been a long time ill before the heart gets into serious difficulty, when cloudy swelling or other degeneration has been set up, which makes the drug dangerous. Cardiac failure in pneumonia, however, if it occur at all, shows itself within eight or ten days, within which time serious muscle change can hardly have occurred; hence, I believe, its great usefulness when needed in pneumonia. If the stomach is acting badly, or the tongue dry and brown, it had better be given hypodermically.

Oxygen, while probably more useful in bronchopneumonia or capillary bronchitis than in true pneumonia, has its place as a cardiac stimulant, and probably assists in reducing toxemia.

The indications for alcohol in this as in any other acute infection are, I think, the presence of two or more of the following conditions: (1) Dry brown tongue; (2) marked delirium, especially of the low muttering type; (3) a rapid and rising heart rate; (4) high temperature.

I would oppose its routine use, but where indicated as above it should be used, and if used at all, pushed boldly for twenty-four hours, after which if no improvement be noted, it had better be gradually withdrawn and caffeine or perhaps camphor dissolved in oil substituted.

OPIATES. The use of opium in any form constitutes one of the most important questions in the management of this disease. My own rules about it are as follows: (1) Even minute doses are dangerous at either extreme of life. (2) Use it in no case in which there is much bronchitis, edema, or other abnormal condition of the non-consolidated portions of the lung. (3) Avoid it when marked cyanosis exists, especially with pallor and sweating, and tympanites.

The main conditions calling for an opiate are severe pain, marked sleeplessness and restlessness, and threatening cardiac failure. In the latter case, very small doses are best, say gr. $\frac{1}{32}$ repeated.

Pain, for instance, can usually be controlled by the poultice or ice bag, preferably the latter in the adult, or by leeches, and it at any rate usually occurs early if at all when one or two doses of morphine are less likely to be harmful. The drug tends to favor toxemia by locking up the bowels, which must be guarded against, as already indicated, by purgatives.

COMPLICATIONS. In regard to complications, one can best foresee and guard against these by having a clear conception, to be obtained only by experience, of the average standard case of pneumonia. The composite photograph carried in one's mind, the result of careful study of perhaps 100 cases, would lead one to expect a temperature of 103° F., a pulse less than 120, and a breath rate less than 40. Any departure from this ratio should be carefully watched.

For the control of fever, cool air, light clothing, the use of the ice bag or cold sponge in adults, the hot pack in children, should suffice. Antipyretics should rarely if ever be used, as transient in their effects on the fever and depressing to the heart; and of course nothing in the treatment should be permitted which tends even remotely to induce cardiac failure. I cannot, however, refrain from mentioning a series of cases of acute pneumonia which I once saw in camp with the 5th Battalion, the Royal Warwickshire Regiment, in England. They were all strong young sthenic cases and they lay on stretchers in an open marquee in hot weather in August, with nothing but milk and water to drink, and one might almost say phenacetin to eat. They all made excellent recoveries. Under

ordinary conditions such treatment would be impossible. It must be remembered, also, that moderate fever is a reparative process meant to stimulate leukocytosis and phagocytosis, and constituting a most important phase of the reaction to the infection. Quinine in single doses, 20 to 30 grains, is not depressing, although sometimes nauseating; and alcohol, as above mentioned, serves to spare tissue waste when fever is high. Other complications, such as delirium, abdominal distention, and declining blood pressure, have already been noted, and in this paper cannot be referred to at greater length. Neither is it within the scope of this article to discuss such complications as pericarditis, empyema, or other pleural effusions, lung disease or gangrene, meningitis, neuritis, arthritis, or phlebitis; each calls for its own special treatment, and while bearing in mind that the case is still one of pneumonia, one should neither lose hope nor abandon treatment because of the appearance of any of them.

It is superfluous to emphasize our modern views as to the necessity of fresh air, proper restriction of dietary, and the non-necessity of the poultice except for pain. Popular prejudice, of course, especially in private as against hospital practice, often denies us a free hand in the nursing details, as we all know that on many occasions when the patient dies the open window and the ice-bag, or underfeeding, or overuse of alcohol, will all be blamed by the friends as the cause of death.

Finally, with regard to convalescence: let me remind you of the dangers that attend the crisis, particularly in the aged. How often has one been grievously disappointed, especially in the case of the old, by death from cardiac failure just after the storm seems to have been weathered; and even in a sthenic case, where a critical fall of temperature is not accompanied by much danger to the heart, and the marked return of the sense of *bien-être* has made the patient anxious to be early out of bed, it is well to insist upon at least ten days' convalescence in bed: (1) To allow the heart to recover its proper tone; (2) to avoid risk of empyema, especially if there has been extensive pleurisy, and to allow complete resolution, for the lung tissue remains tender for at least that length of time after the patient's strength has begun to return.

In conclusion, it will be seen that although at too great length, I have not attempted to treat the subject exhaustively.

THE ANATOMICAL EXPLANATION OF THE RELATIVELY LESS RESONANT, HIGHER PITCHED, VESICULOTYMPANITIC PERCUSSION NOTE NORMALLY FOUND AT THE RIGHT PULMONARY APEX.¹

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Most clinicians, especially those who have devoted particular attention to diseases of the lungs, are agreed that in percussing the upper parts of the chest a slight difference in sound is normally heard when the two sides are compared. This difference consists in the fact that on the right side, from the apex down to about the level of the second interspace or the third rib, the note elicited is slightly higher in pitch, shorter in duration, and less resonant. Occasionally, also, the note is somewhat more tympanitic in quality.

The actual amount of difference in the afore-mentioned sound attributes, while never great in degree, is of extreme clinical importance on account of the frequency with which incipient tuberculosis manifests itself by physical signs at the right apex. If no allowance be made for a normal variation in the percussion sounds of the two sides of the chest, errors in diagnosis easily may occur.

On consulting various text-books on the subject one finds that in reference to the question under consideration they may be divided into four classes: (1) Those in which allusion is made to the difference, but no explanation is offered. (2) Those in which no mention of any difference is made. (3) Those in which it is denied that any difference exists. (4) Those in which more or less explanation of the phenomena is attempted.

The following statements are taken from works on physical diagnosis which comprise the first class:

"On the right side the sound is somewhat less clear, shorter, and of a higher pitch than on the left." (J. M. DaCosta.²)

"The pulmonary quality is slightly less marked on the right

¹ Read before the College of Physicians of Philadelphia, January 3, 1912.

² Medical Diagnosis, 1900, p. 270.

than on the left in supraclavicular and infraclavicular areas." (G. R. Butler.³)

"It [the resonance] is slightly higher in pitch at the right than at the left apex." (J. H. Musser.⁴)

Similar statements are made by J. C. Wilson⁵ and R. C. Cabot.⁶

Among the authors who make no mention of the normal variation in the percussion note of the two sides are: Loomis,⁷ Gibson and Russell,⁸ Vierordt,⁹ J. H. Bass,¹⁰ P. Simon,¹¹ S. Gee,¹² A. Weil,¹³ P. Niemeyer,¹⁴ Ebstein,¹⁵ Stokes,¹⁶ Sahli,¹⁷ Hare,¹⁸ Fowler and Godlee,¹⁹ and Fuller.²⁰

In the third class we found only one book, that by S. G. Bonney,²¹ who says, "The characteristics of normal resonance are identical upon the two sides of the chest in this (infraclavicular) region, as contrasted with the striking differences displayed below the third ribs."

The text-books of the fourth group offer numerous explanations of the phenomena.

The explanation is based on the thickness of the pectoral muscles by the following writers: A. Flint,²² J. G. Brown,²³ Edlefsen,²⁴ Beevor,²⁵ Guttman,²⁶ E. Cassaët.²⁷

Eichhorst²⁸ says that the difference is most marked in men of laborious occupations. He goes on to say, however: "Bei Linkshaendigen habe ich den Perkussionsschall beiderseits laut gefunden."

Brugsch and Schittenhelm²⁹ and C. L. Greene,³⁰ regard the difference as due to the nearness of the large bronchus.

Kidd³¹ attributes the variation in part to the difference in the

³ The Diagnostics of Internal Medicine, p. 426.

⁴ A Practical Treatise on Medical Diagnosis, 1899, p. 495.

⁵ Medical Diagnosis, 1909, p. 131.

⁶ Physical Diagnosis, 1909, p. 130.

⁷ Lessons in Physical Diagnosis, 1887, p. 27.

⁸ Physical Diagnosis, 1902, p. 142.

⁹ Lehrbuch d. klin. Untersuchungsmethoden, 1904, i, 112 and 634.

¹⁰ Medizinische Diagnostik, 1883, p. 112.

¹¹ Man. de Percussion et d'Auscultation, 1895, p. 35.

¹² Auscultation and Percussion, 1907.

¹³ Handbuch u. Atlas der Topograph, Perkussion, 1877, p. 42.

¹⁴ Handbuch d. theor. u. klin. Perkussion u. Auscultation, 1870, p. 130.

¹⁵ Leitfaden d. Aerztlichen Untersuchung, etc., 1907, pp. 151 to 158.

¹⁶ Diagnosis and treatment of the Diseases of the Chest, 1837, Part 1.

¹⁷ A Treatise on Diagnostic Methods of Examination, 1905.

¹⁸ Practical Diagnosis, 1906.

¹⁹ Diseases of the Lungs, 1898.

²⁰ Diseases of the Lungs and Air Passages, 1867, p. 51.

²¹ Pulmonary Tuberculosis, Philadelphia, 1903, p. 183.

²² Variations of Pitch in Percussion and Respiratory Sounds, 1852, p. 9.

²³ Medical Diagnosis, Edinburgh, 1887.

²⁴ Lehrbuch d. Diag. d. inn. Krankheiten, 1889, p. 449.

²⁵ Lancet, May 4, 1901, p. 1275.

²⁶ Lehrbuch der Klin. Untersuchungsmethoden (Klemperer), 1904, p. 145.

²⁷ Precis d'auscultation et de Percussion, 1906, p. 563.

²⁸ Lehrbuch d. Physikal. Untersuchungsmethoden, Berlin, 1889, i, 269.

²⁹ Lehrbuch Klinischer Untersuchungsmethoden, 1903, p. 80.

³⁰ Medical Diagnosis, 1910, p. 101.

³¹ Allbutt's System of Medicine, 1909, v, 346.

bronchi, stating that the right main bronchus is slightly wider and more vertical, and that the bronchus to the upper lobe is given off higher up, that is, near to the trachea.

In answer to this it may be stated that the point at which the upper lobe bronchus of the right side is given off is opposite the upper border of the third costal cartilage. Its effect on resonance at the apex must be very slight.

Walshe³² states that "In a certain number of persons whose lungs are perfectly sound the right infraclavicular region gives a more wooden note under percussion, and is at the same time less resonant than the left. This peculiarity is perfectly unconnected with excess of muscular substance on the right side, and depends on some hitherto unascertained condition."

In another place³³ the same author writes that: "Numerous differences in the results of percussion of corresponding points of the two sides of the chest have been noticed, and traced to an obvious cause the presence of texture and organs of different densities in those spots. Variable thickness of the external soft parts will have a similar effect; thus the right infraclavicular region is less resonant than the left in robust persons whose employment requires much use of the right arm; the pectoralis muscle enlarges from use. Here the explanation is obvious, but the explanation is not obvious when the right infraclavicular region emits less tone than its fellow, in persons presenting no muscular thickening of this kind. Such inferiority of resonance (sometimes attended, too, with slight elevation of pitch) is never great provided the lungs are perfectly healthy; it holds good whatever be the direction given to the fingers, and whether they fall outward toward the humerus or inward toward the sternum."

H. S. Anders³⁴ attempts an explanation by stating that in addition to greater thickness of the pectoral muscle and the presence of the liver on the right side, "an explicit reason is found in the fact that there is a different anatomical arrangement of the bronchial tubes, those on the right side being larger and situated more superficially and higher up; this, with a bunch of medium and small branches occupying space, that on the left side is filled with air vesicles, gives an amount of bronchovesicular tissue sufficient to elevate the pitch slightly but perceptibly, the tubes adding an element of tympany, the extra muscular and connective tissue of their firm walls an element of dulness."

Anders and Boston³⁵ state: "The higher pitched percussion note over the right than over the left apex is probably due to larger diameter and higher position of the right bronchus. The note is again modified by the thickness and tension of the chest wall as the result of muscular contraction, etc."

³² Practical Treatise on the Diseases of the Lungs, 1871, p. 64.

³³ Lancet, 1849, i, 196.

³⁴ Text-book of Medical Diagnosis, 1911, p. 55.

³⁵ Physical Diagnosis, 1907, p. 99.

Gerhardt³⁶ offers the following reasons: (1) Increased size of the muscles on the right; (2) slight scoliosis often present; (3) difference in anatomical structure: (a) bronchi larger, (b) pulmonary apex smaller and lower, (c) bronchi retain large caliber near to the surface.

TABLE OF RESULTS OBTAINED BY EXAMINING THE CHESTS OF THIRTY-TWO LEFT-HANDED INDIVIDUALS.

No.	Circumference of chest (inches)		Vocal fremitus		Percussion resonance		Pitch (higher)		Breath sounds (harsher)		Remarks
	R	L	R	L	R	L	R	L	R	L	
1	17¼	17	+	..	-	..	+	..	Equal		Poorly developed; 18 yrs. old; looks to be 14.
2	14½	14	+	..	-	..	+	..	Equal		
3	16¼	16	+	..	-	..	+	..	+	..	Large deep pectoral muscles; difference only on deep percussion.
4	18¾	18	+	..	-	..	+	..	+	..	
5	16	15¼	+	..	-	..	+	..	+	..	Large left pectoral muscles; difference slight. Well marked difference.
6	16½	16½	+	..	-	..	+	..	+	..	
7	17½	17¾	+	..	-	..	+	..	+	..	Bilateral subclavian murmur. Difference slight. Funnel breasted.
8	16½	16¾	+	..	-	..	+	..	+	..	
9	15¾	16¼	+	..	-	..	+	..	+	..	
10	16	16	+	..	-	..	+	..	+	..	
11	15½	15¾	+	..	-	..	+	..	+	..	
12	17¾	17½	+	..	-	..	+	..	+	..	Marked retraction of whole right side.
13	15½	16	+	..	-	..	+	..	+	..	
14	16½	16½	+	..	-	..	+	..	+	..	Flat left chest; looks pathological.
15	17¾	17½	+	..	-	..	+	..	+	..	
16	16	16	+	..	-	..	+	..	+	..	
17	18	17	+	..	-	..	+	..	+	..	
18	17	16½	+	..	-	..	+	..	+	..	
19	16½	17½	+	..	-	..	+	..	+	..	
20	17¾	18¼	+	..	-	..	Equal	+	+	..	
21	16½	18	+	..	+	..	+	..	-	+	
22	18¼	18½	+	..	-	..	+	..	+	..	
23	15½	15¼	+	+	..	+	Equal		Very poor expansion; feeble breath sounds.
24	18½	18½	+	..	-	..	+	..	Equal		
25	18¾	18	+	..	-	..	+	..	+	..	
26	17	17	+	..	-	..	+	..	+	..	
27	16½	17	+	..	-	..	+	..	+	..	
28	15¾	15¾	+	..	-	..	+	..	+	..	
29	16	15¾	+	..	-	..	+	..	+	..	
30	18½	18	+	..	-	..	+	..	+	..	Difference reversed on light percussion.
31	18	17½	+	..	-	..	+	..	+	..	
32	16¾	16¾	+	..	-	..	+	..	+	..	

Inasmuch as none of these explanations are adequate to account for all cases, we have endeavored to solve the problem by the careful anatomical study of frozen sections of the cadaver, previously hardened in formalin, and by a critical study of the chests of 32 left-handed students. The examinations of the left-handed individuals were made with especial reference to the following points: (1) Circumference of the chest, right and left. A tape-measure was applied to the side of the chest, extending from the middle of the spine to the mid-sternum at the level of the nipple. For obvious reasons errors in such measurements may easily be made, and we, therefore, lay no great stress on the importance of the data thus obtained. The results show, however, that the *right* chest is not infrequently larger even in left handed-persons. (2) Vocal fremitus, elicited below the clavicle. (3) Percussion resonance, from the clavicle to the upper border of the third rib. (4) Percussion pitch, elicited over the same area. (5) Character of the breath sounds in the same region. Corresponding points on the two sides of the chest were of course compared, and the results immediately recorded.

The foregoing table represents in charted form the results of our examinations, and the data obtained were so uniform that it seemed needless to examine a larger number of men. From these studies the following conclusions may be drawn:

Vocal fremitus is normally more intense on the right side, even in left-handed individuals, and probably is due, as was pointed out by one of us (Fetterolf³⁷), to the immediate contact of the trachea to the right pulmonary apex. On the left side the aorta, the common carotid and subclavian arteries, and the esophagus, together with lymphatic and areolar tissue, a layer some 2 to 3 cm. in thickness, are interposed between the lung and the trachea.

While studying the percussion sounds at the two apices it was occasionally noted that after prolonged percussion differences quite noticeable at first tended to become less marked. This is by no means an original observation, and may be explained as due to one or all of the following factors: (1) Aural fatigue on the part of the examiner. (2) A pulmonary reflex, as described by Abrahms, by virtue of which percussion over a certain area of lung tissue produces a local reflex dilatation of the air vesicles, thus obscuring a slight degree of dulness. (3) Spasm of the deeper fibers of the pectoral muscle, analogous to the increased myotatic irritability of myoedema seen in low nerve tone,³⁸ which by increased muscular density tends to limit the penetration of the percussion vibrations.

In persons of poor muscular development, in case of the aged, the wasted, and the muscularly inactive, the difference in the

³⁷ Arch. Int. Med., February, 1909.

³⁸ This explanation, used in a somewhat similar connection, has been suggested by M. E. Rist, Percussion Thoracique, La Presse Medicale, December 16, 1911.

pulmonary resonance is present, while a corresponding unevenness in the thickness of the pectoral muscles may be either inconsequential or entirely lacking. The main cause, then, must lie deeper than in the muscles of the chest.

Let us consider for a moment what physical conditions underlie the changes in the percussion note which we are endeavoring to explain, namely, (1) diminished resonance; (2) elevated pitch; (3) a tympanitic element.

1. *Diminished resonance* over normal lung implies a lessened quantity of air and elasticity or the presence of overlying tissue, which by reason of its density vibrates less complexly, and transmits vibrations less well. The result, acoustically speaking, is a condition in which the fundamental note preponderates and fewer overtones are heard. The sound is more muffled and is shorter and weaker, tone enforcement being diminished. With the appearance of dulness there is always an increase in the elevation of pitch.

2. *Elevation in pitch* implies an increased vibratory rate, and this in normal pulmonary tissue again depends largely, other things being equal, on the amount of air, the size of the air columns.

3. *A tympanitic quality* is heard over pulmonary tissue when: (a) Air columns vibrate in smooth walled chambers which communicate with the atmosphere; (b) when air in closed cavities vibrates in unison with elastic walls; (c) when the normal pulmonary tension is relaxed, so that the lung vibrates as a whole (for example, in pleural effusion). Acoustically the underlying characteristic of tympany is preponderance of overtones. For the present purposes only the first proposition (a) need be considered.

It may be stated as a general principle that a less resonant note is produced by an increase in the amount of airless tissue. Writers who have hitherto considered this to be a factor, have confined their explanation to conditions of the chest wall, assuming that right-handed people have so much more muscular tissue over the pulmonary apex on that side, that the percussion note becomes dulled in quality. Thus two left-handed individuals were exhibited before the Clinical Society of London by Sir Hugh Beevor to prove this very point, that is, that the left side was less resonant.³⁹ Similar conclusions were reached by Brazil,⁴⁰ who, having studied a number of cases, states that the higher pitched note on the left, in left-handed people affects the entire chest, and is not limited to the apices. How this can be it is difficult to understand, because in the axillary region, for example, muscular development plays practically no role.

Similar views are held by E. Lloyd Jones,⁴¹ who in an interesting article quotes as corroborative evidence the fact that in a right-handed patient of his the left side was less resonant than the

³⁹ Lancet, May 4, 1901, p. 1275.

⁴⁰ Brit. Med. Jour., October 26, 1899, p. 920.

⁴¹ Brit. Med. Jour., October 24, 1903.

right on account of a "former venous thrombosis in the left arm," the veins in the upper part of the left chest being much enlarged. It seems to us that Jones' explanation, which links a diminished resonance with the presence of thrombotic vascular changes on the left side, is in entire consonance with the explanation proposed in this communication. We believe, however, that the percussion changes in such a case as he reports are due more to a distention of the large vessels crossing the apex than to a thickening of the superficial tissues.

AUTHORS' EXPLANATION.

As the result of our studies we believe that the anatomical basis for the conditions under discussion consists of three factors, namely, the anterior position of the vessels in relation to the right apex as compared with the left, the consequent encroachment upon and reduction in size of the right apex, and the apposition of the trachea to the inner surface of the right apex, while the same aspect of the left is in contact with a thick layer of solid tissue.

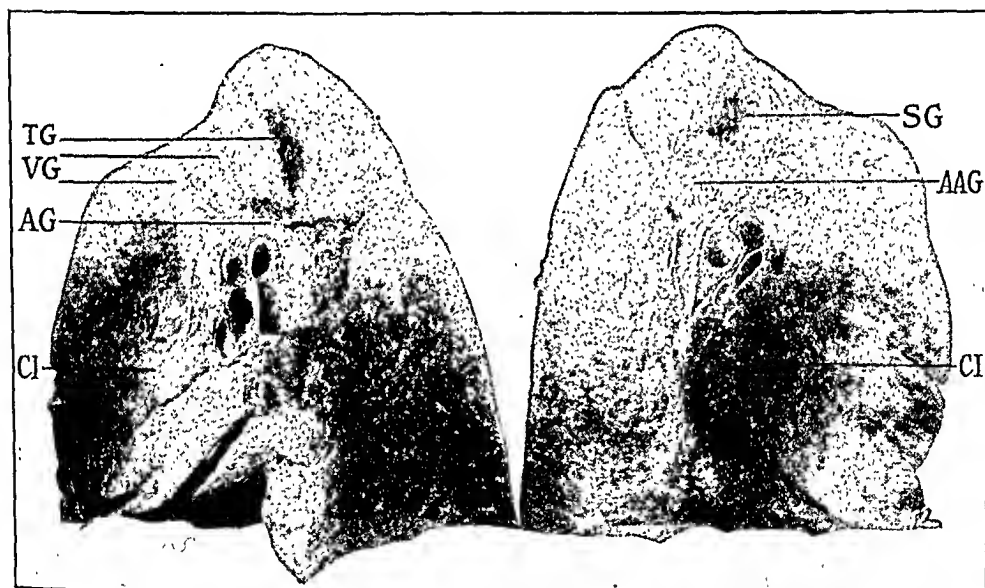


FIG. 1.—Mediastinal surface of lungs hardened before removal. This photograph shows (a) the groove produced in the right apex by the trachea; (b) the relatively anterior position of the vessels on the right side; and (c) the smaller size of the right apex. AG, azygos groove, VG, grooves for superior vena cava, innominate vein, and subclavian vessels; TG, tracheal groove; SG, subclavian groove; AAG, aortic groove; CI, cardiac impression.

Reduced to their last analysis the anatomical differences between the two sides in the upper thorax will be found to be due to the fact that man is a sinistro-aortic individual. In some of the lower vertebrates, for example, the birds, the aorta is on the right side, and in others, as some of the lizards, there is an aorta on both sides.

In the early human embryo, when the heart is situated far forward in the pharyngeal region, the arrangement of the large arteries is

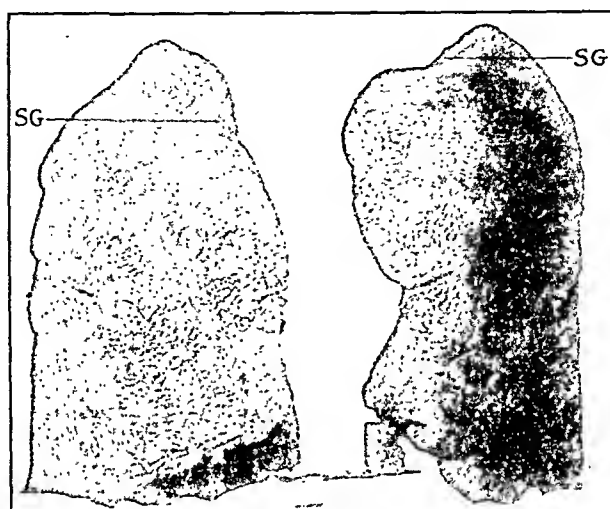


FIG. 2.—Anterior view of lungs hardened before removal. This photograph shows the anterior position of the groove for the subclavian vessels on the right side, compared with the more superior position on the left. SG, subclavian groove.



FIG. 3.—Lateral view of lungs hardened before removal. This photograph shows the deeper vascular groove and the smaller size of the right apex as compared with the left.

symmetrical. As development proceeds the main trunk, the aorta, is established on the left side.

In its course from the heart to the vertebral column the systemic aorta passes first slightly to the right, then slightly to the left, and finally almost directly backward between the left side of the trachea and the mediastinal aspect of the left lung. Thus situated it affects both the trachea and the lung, throwing the lower end of the former over toward the right, thereby producing the now well recognized dextro-inclination of the trachea, and grooving deeply, in an arciform manner, the inner aspect of the left lung, in front, above, and behind the root of the latter.

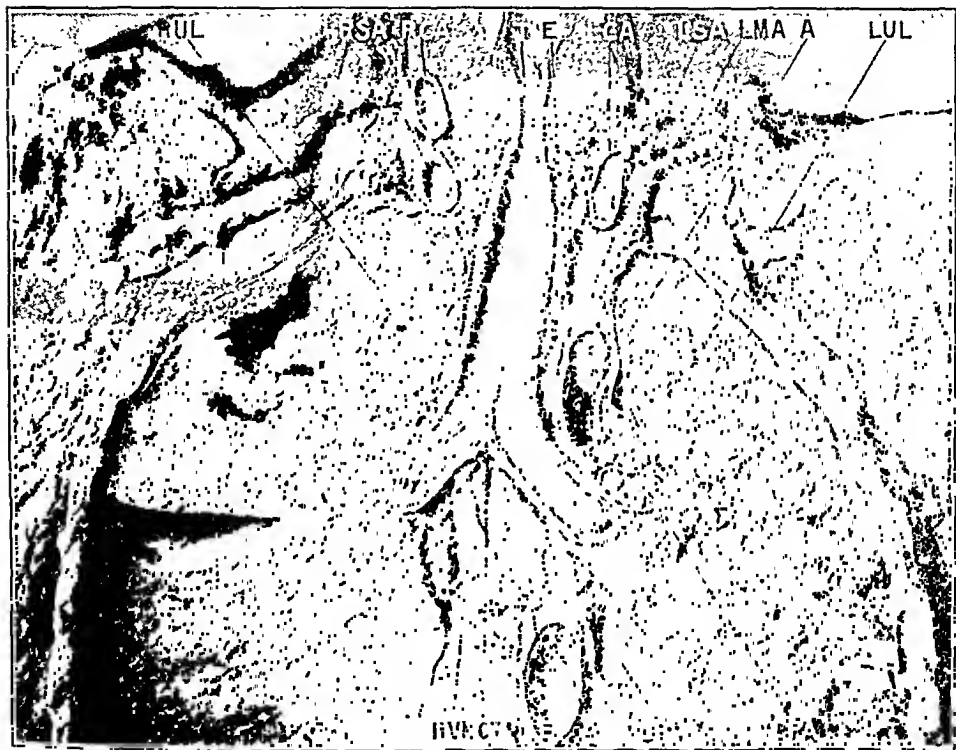


FIG. 4.—Frontal section of the thorax in the axis of the trachea. This photograph shows (a) the contact of the right upper lobe with the trachea, (b) the mesial position of the left subclavian artery in relation to the left upper lobe, and (c) the essentially anterior position of the right subclavian in relation to the right upper lobe. *RUL*, right upper lobe; *RSA*, right subclavian artery; *RCA*, right common carotid artery; *T*, trachea; *E*, esophagus; *LCA*, left common carotid artery; *LSA*, left subclavian artery; *LMA*, left internal mammary artery; *A*, aorta; *LUL*, left upper lobe; *LPV*, left inferior pulmonary vein; *CT*, carina tracheae; *RVN*, right vagus nerve. (Reproduced from the Archives of Internal Medicine, February, 1909.)

The aortic arch is usually divided by writers into three portions, an ascending, a transverse, and a descending. The first and third of these parts are properly named, but "transverse" is incorrectly applied to the second portion. As regards the aorta, it should be abolished from anatomical terminology and some such term as "horizontal" substituted for it. Its use in this connection probably originated from the fact that when the chest is opened under ordinary condition, the collapsed lungs and the heart fall backward,

and the second portion of the arch becomes approximately transverse. But when the thoracic contents are hardened before the chest is opened it is seen clearly that there is no justification for applying to the second part the term "transverse." When examined under such conditions the general course of the aortic arch is seen distinctly to be almost anteroposterior, there being, of course, a slight tendency to run toward the left. This is demonstrated most clearly in all of the sections that we have prepared; and in nearly all of those cut in the sagittal plane the entire aortic arch from beginning to end is included in the section.

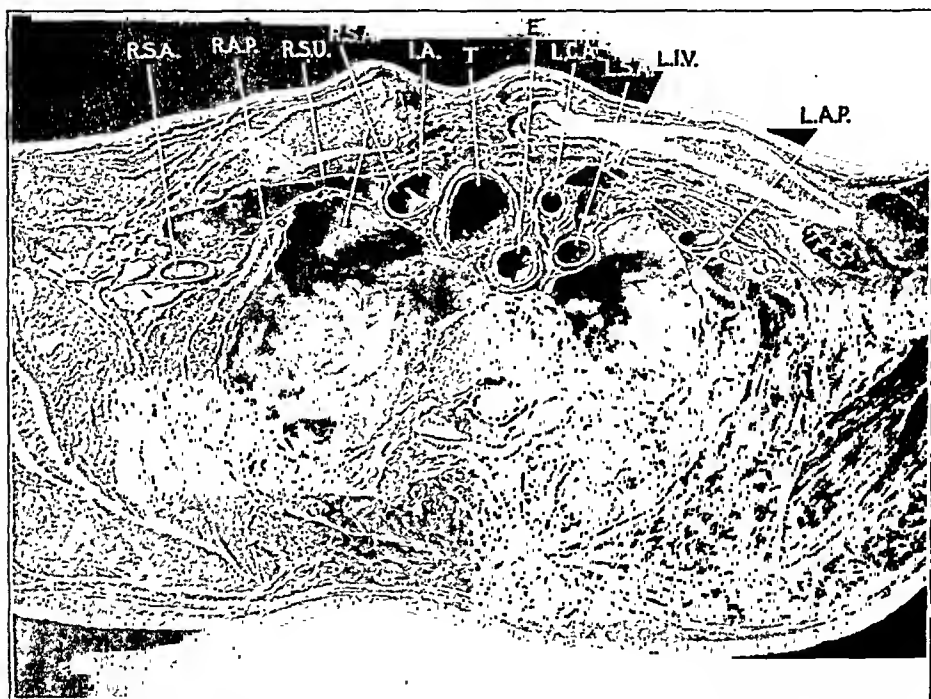


FIG. 5.—Section through the upper part of the thorax, viewed from below. The line of section is not exactly horizontal, a slightly lower plane being reached on the right side than on the left. In order to show the apical parietal pleura, the pulmonary apices have been removed. There can be noted in this specimen the beginning contact of the right pleura with the trachea, and the anterior position of the innominate artery, whose bifurcation is well shown. On the left side, the wide separation of the pleura from the trachea by means of the large arteries, esophagus, and areolar tissue can readily be seen. There can be seen well the deep position of origin and the obliquely anterior course of the left subclavian artery. T, trachea; E, esophagus; RAP, right apical pleura; LAP, left apical pleura; IA, innominate artery, dividing into RSA, right subclavian artery and RCA, right common carotid artery; LSA, left subclavian artery; LCA, left common carotid artery; RSV, right subclavian vein; LIV, left innominate vein.

As stated above, we believe that there are three ultimate factors at work to produce the normal discrepancies at the apices.

First. As regards the anterior position of the vessels of the right side. The first branch, better called the anterior branch, of the horizontal part of the aortic arch is the innominate artery, destined for the supply of the right head and the right upper extremity. Arising, as it does, to the left of the median line, it is compelled to

pass anterior to the trachea in order to reach its destination. This position of its origin is responsible for the anterior situation of the vessels in relation to the right apex. Having crossed the anterior aspect of the trachea and turned somewhat posteriorly, it divides into its terminal branches, the right common carotid and the right subclavian, the former of which does not concern us. The latter passes obliquely upward and *backward* to reach its groove on the upper surface of the first rib. In its course it produces a deep sulcus in the anterior aspect of the pulmonary apex.

The second brach of the horizontal part of the arch is the left common carotid. It passes upward at the side of the trachea, between the trachea and the left apex, and enters the neck.

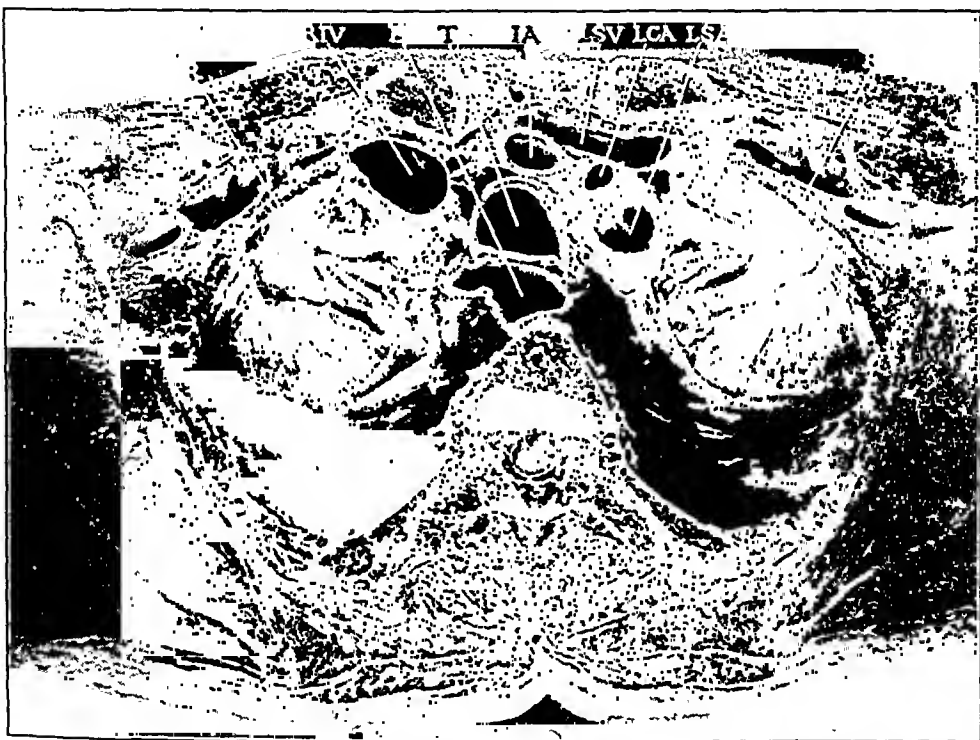


FIG. 6.—Horizontal section of the thorax just above the sternoclavicular articulation. The pleura has been dissected away. This photograph shows (a) the anterior position of the innominate artery, (b) the posterior position of the left subclavian artery, and (c) the anterior position of the right innominate vein. *R*, first rib; *RIV*, right innominate vein; *E*, esophagus; *T*, trachea; *IA*, innominate artery; *LSV*, left subclavian vein; *LCA*, left common carotid artery; *LSA*, left subclavian artery.

The third or posterior branch of the horizontal part of the arch is the left subclavian. This vessel is given off well back in the mediastinum, opposite the posterior surface of the trachea, or even at the left side of the esophagus. It arises so deeply that it is compelled to pass slightly *forward* as well as laterally to reach its groove on the first rib. In the greater part of its thoracic course it occupies the layer of tissue between the left upper lobe and the trachea. Nearing the first rib it produces in the left apex a groove which is shallower and nearer the summit than on the right side.

The same principle applies to the veins. The right apex is encroached upon and markedly grooved by the subclavian and innominate veins, these grooves being continuous with one another, and situated in front of the groove for the subclavian artery. On the left side the subclavian vein produces a sulcus in front of that of the artery, but being more mesial it does not encroach to so great an extent on the apex.

Second. The smaller size of the right apex as compared to the left. This is dependent on the facts enumerated in the previous section. On the right side the vessels pass in front and occupy space which on the left side is occupied by lung tissue.

The shape and size of the pulmonary apices are modified by the vessels in the same way as would be two small hills over which roads were cut. In one case, as on the right side, the road is cut over the side of the hill and requires excavation. On the other side, corresponding to the left apex, the road is carried more nearly over the summit and comparatively no excavation is needed. The result, as far as the apices are concerned, is to cause the former to be smaller than the latter and to give the right apex a more conical, and the left a more dome-like shape.

Third. The apposition to the inner surface of the right apex of the trachea and to the left of solid tissue. This has been emphasized by one of us in a previous paper,⁴² and is demonstrated clearly in Figs. 4 and 5.

CONCLUSIONS.

1. The dexterity of the individual has no effect on either the vocal resonance and fremitus or on the percussion pitch and resonance at the apices.

2. The percussion note in the healthy individual is practically always less resonant and higher pitched at the right apex, except in the presence of unusually well-developed left pectoral muscles, and then only if very light percussion is employed.

3. The normal differences are due to the anterior position of the large vessels in relation to the right apex, as compared with the left, to the consequent encroachment upon and reduction in size of the right apex, and to the contact of the inner surface of the right apex with the resonating trachea, while the left is in contact with non-resonating solid tissue.

4. The differences are most marked anteriorly and mesially, because in this situation both trachea and vessels would exert their greatest influence, less marked posteriorly and mesially where the influence of only the trachea would be present, and least marked laterally, since the outer portion of the apex is farthest removed from the trachea, and the vessels at this point are practically similar in their relations on the two sides.

We wish to express our indebtedness to Dr. George A. Piersol for anatomical material placed at our disposal, to Dr. R. Tait McKenzie for the privilege of examining a large number of left-handed students, and to Dr. P. G. Skillern, Jr., for assistance in preparing our anatomical specimens.

RUPTURE OF THE KIDNEY IN CHILDREN.¹

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RUPTURES or other subcutaneous injuries are very uncommon in children, only 22 cases being reported in tabulated statistics.² My experience comprises 4 cases of complete rupture of the kidney in children, aged from eight to twelve years, and a consideration of the conditions found furnishes some interesting features.

CASE I.—Barbara S., aged ten years. Admitted to St. Luke's Hospital August 25, 1902. Two weeks ago was kicked on the right side of the body by a horse; unconscious for a while. Next morning urine contained some blood, none seen since. Some swelling of the right side developed with a considerable amount of pain. Has had no chills, but there have been fever and sweating.

Physical examination showed a bright, healthy child, with a visible swelling of the right lumbar region. No superficial discoloration. The swelling was elastic, insensitive to pressure, flat on percussion. Urine: acid; 1018; no albumin.

Operation: Right lumbar incision, showed the swelling to be a large retroperitoneal accumulation of normal appearing urine. The kidney was ruptured in two, the lower pole entirely separated from the upper three-fourths of the viscus. Nephrectomy; good recovery. Discharged October 3, 1902.

CASE II.—These details are as exact as I can furnish them from memory, the record being lost. Boy, aged about ten years. Admitted to the Hudson Street Hospital probably in the summer of 1907. Runover injury; abdominal symptoms; median laparotomy by a colleague; negative findings. Seen by me several days later; diagnosis of rupture of left kidney. Lumbar incision revealed complete tear of left kidney. Nephrectomy; good recovery.

CASE III.—James L., aged twelve years. Admitted to the Hudson Street Hospital November, 1909. While running across the street an automobile struck him in the left side, knocking him down. Scalp wound, requiring two stitches. Brought to the hospital in the guilty automobile. Soon began to complain of great pain and tenderness over the left kidney region.

¹ Read before the Section of Surgery of the New York State Medical Society, April 17, 1912.

² Watson and Cunningham. *Genito-urinary Diseases*, vol. ii.

Physical Examination: Tenderness and rigidity in left hypochondrium, also some slight discoloration. Skin and mucous membranes of good color. Shortly after admission passed blood-tinged urine. Hemoglobin, 70 per cent. Operation about eight hours after injury; left lumbar incision; complete rupture of kidney into two pieces. Nephrectomy; drained, good recovery; highest temperature, 100.5° F. Discharged in three weeks.

CASE IV.—M. S., girl, aged eight years. Admitted to St. Luke's Hospital, July 16, 1910. Complained of pain in the "stomach." Two days before she had fallen a distance of four and a half feet, landing on the ground on the right side. Went home; complained of pain in her stomach, which has continued ever since. Bowels regular. No trouble with urination; no blood in the urine; has vomited twice.

Physical Examination: Negative except for the abdomen, which shows general rigidity with tenderness on the lower right side. Temperature, 102° F. Blood count: Leukocytosis, 25,000; polynuclears, 88 per cent. No urine record. Probable diagnosis, appendicitis. Immediate operation. Intermuscular incision; on separating the muscles a considerable amount of fluid was evacuated. On opening the peritoneum a similar fluid escaped from the pelvis. The cecal wall was the site of a considerable ecchymosis. Appendix normal (removed). The wound was dilated retroperitoneally, to allow of a sponge being pushed up into the lumbar region; it returned bloody, but without evacuating any fluid. Injury to the kidney seemed probable; it could be palpated quite readily, but no obvious abnormality being detected (intracapsular rupture) it was decided to await further developments.

The child recovered well and seemed relieved. The urine the next day (July 17): Neutral; 1034; a very faint trace of albumin; a few hyaline casts were present.

July 20. Urine: Acid; 1014; very faint trace of albumin; a few leukocytes.

July 21: Urine: acid; 1020; albumin, 10 per cent.; many red blood cells. In view of this last urine report, exploration was undertaken. Right lumbar incision; the true capsule was found intact, but distended with blood, and raised from the kidney; on opening it, the kidney was found broken completely in two; lower smaller fragment showed beginning necrosis. Nephrectomy; drainage; perfect recovery. Discharged August 9.

This case is interesting, showing a complete rupture resulting from a relatively slight trauma, leaving no mark on the body and producing absolutely no shock, the masking of kidney symptoms by the bruising of the lower abdominal muscles and the colon, the absence of any urinary symptoms until five days after the injury, and also that the kidney may be divided completely in two without appreciable solution of continuity of its capsule.

Four complete ruptures of the kidney in children, aged under twelve years, occurring in the practice of one surgeon seems unusual in view of the small number of such cases on record. It is possible that these cases are really not so rare, and may be overlooked with disastrous results by those who hesitate to interfere in dubious cases. The similarity of the lesions is interesting, being exactly alike in all 4 cases; complete division of the viscus in two parts, the lower one being the lesser. In one instance the capsule remained untornd.

The fact that the kidney lesions were the same with the different kinds of violence seems to confirm the theory of "bursting" by hydraulic pressure. Also the line of rupture; vertical to the long axis at about the junction of the two lower thirds would seem to indicate that we had here an instance of a definite line of least resistance such as I have not seen indicated in any treatise on the subject.



Ruptured kidney. Case IV.

Although the lesion in all these cases was severe, the symptoms, on the whole, were mild, and in several ways deficient. Nephrectomy was necessary in every instance, and successful; no other operation would have been permissible. Three of the children have been under observation and have remained well.

As regards the etiology of such severe injuries, it is obvious that children are relatively little exposed to the various forms of trauma commonly encountered by active men (96 per cent. of all cases). Most modern observations seem to corroborate Küttner's view that the kidney being a semifluid body bursts along the line of least resistance according to the law of hydraulics. Direct pressure from the lower ribs can also explain it. It is less easy, however, to understand the effects of indirect violence, as from a fall on the feet. A point, however, to be borne in mind, illustrated in 2 of my cases, is that the severest form of damage may result from an injury unaccompanied by marks of external violence on the surface of the body in the kidney region or anywhere else. Possibly in some children a persistence of the infantile ptosis³ may persist leaving

³ Aglave, Bulletin de la Soc. d'Anatomie de Paris, 1910, p. 595.

more of the surface unprotected by the thoracic bulwark. The particular vulnerability in childhood has also been ascribed to the minimum deposit of perinephric fat and the greater tension of the overlying peritoneum.

The extent of the lesion naturally runs the gamut from the mildest of superficial bruises to the complete rupture observed in my 4 cases, to the tearing away of the kidney from its vascular pedicle or the ureter or complete pulpyfying from extraordinary crushes. In the less extensive injuries it is of practical importance whether the tear involves or extends into the pelvis; whether larger vascular trunks are destroyed, with resulting dangerous hemorrhage or jeopardizing the future vitality of portions of the organ; whether the injury is subcapsular, and finally, whether there is a coexistent tear of the peritoneum or injury of the contiguous viscera. Unfortunately, few if any of these lesions can be diagnosticated with certainty as regards their extent, particularly at a period when early interference may be all important. A consideration of the nature of the violence is helpful. Injuries resulting from direct violence will probably produce a rupture of the kidney alone by "bursting" violence. Gross direct violence, such as "runover" accidents, are more likely to result in complex lesions. The intensity of the violence is, however, not a trustworthy guide, as shown by Case I, where a complete rupture resulted from the kick of a horse that left no mark on the skin. It must also be borne in mind that a pathological kidney may rupture from the most trivial accident (Watson's case of the woman whose hydronephrotic kidney ruptured from muscular action while she was washing windows).

The loss of blood resulting from any of these injuries naturally varies. Generally speaking, it is rarely sufficient to endanger life quickly; it is rather the constant and recurring hemorrhage that is most to be dreaded. Even with extensive rents of the kidney the integrity of the capsule tends by tension to check extraordinary bleeding.

As regards diagnosis, it may be stated broadly that a diagnosis of some degree of injury to the kidney presents little difficulty. Statistics give a history of hematuria in 80 per cent. of the cases, and certainly with painstaking microscopic urinary examinations this figure would be increased. It will not ordinarily be difficult to exclude lesions of other portions of the urinary tract, for example, of the bladder, practically always complicated by a fracture of the pelvis. The history or evidence of an injury which may implicate the kidney will generally be elicited; pain, tenderness, and eventually more or less pronounced signs of the extravasation of blood or urine, or both in the marked cases will accentuate the diagnosis and also indicate the side involved. For unusual cases and conditions the cystoscope or ureteral catheter may be used; but as a routine these are uncalled for, as well as unwise, and in children can scarcely ever

be used, and if requiring anesthesia had better be replaced by a harmless and more satisfying exploratory and therapeutic lumbar incision.

What is most difficult is to determine the extent of the lesion, and particularly as regards the condition which most urgently call for interference. The initial symptoms with the exception of the degree of shock and hemorrhage do not present any features which sharply indicate the severity of the damage. It is rather on the development and sequence of secondary manifestation that we have to rely or perhaps waste valuable time.

Very severe injuries or very mild ones may be usually diagnosed with readiness, especially with a definite knowledge and appreciation of the nature of the causative violence. For instance, a child is run over by a heavy wagon, as reported by a competent witness; there are extensive marks on the body; there is abundant and early and perhaps immediate hematuria; there is marked shock. Given these conditions there should be a severe laceration of the kidney and perhaps of other contiguous organs, possibly entailing a laceration of the peritoneum overlying the kidney. These complicating conditions may not always be obvious at the outset, although these marked and dangerous symptoms will manifest themselves later—too late probably to remedy them.

On the other hand, a lad may be hit a severe blow in boxing, the so-called "kidney blow." He feels a good deal of pain; may be temporarily dizzy or sick at his stomach; and sooner or later the urine is tinged with blood. Such a history and such findings indicate a trifling condition, requiring no active treatment.

It is, however, the cases of moderate severity, or of incomplete symptoms, that are the most difficult to judge. The degree of initial shock is alone no criterion; it may be intense for a short time, with only a trifling injury; it may be insignificant, or wanting, with the severest damage. The degree of hemorrhage is also misleading. A small vessel may bleed savagely for a while, and if the bulk of the hemorrhage finds a ready escape down the ureter we shall have an alarming picture for a perhaps trifling condition. On the other hand, mechanical obstacles—rupture of the pelvis or ureter (or blocking), clotting, or absence of considerable hemorrhage from the kidney—may result in little hematuria even in the presence of the severest damage.

Absence of visible marks of external violence is no criterion, for complete rupture may occur despite this negative evidence (Cases I and IV).

The significance of a swelling in the flank varies a good deal. If considerable and early it usually means extensive damage. Some of it may be due to the trauma to the abdominal wall, some to the bulk of the extravasated blood, some to the reaction of irritated intestines inhibiting peristalsis, or to an actual lesion of the gut, or

later to a peritonitis due to extravasation of urine, or an infection of the retroperitoneal tissues, or from associated injuries.

The amount of urine collecting in the tissues will depend on whether the injury involves a rupture of (1) the capsule, (2) pelvis, (3) ureter, and whether the urine can accumulate in a well-defined space, or whether opportunity is offered for extravasation into the tissues or the peritoneum. Tuffier has shown from animal experiments, and clinical observations have corroborated, that the lacerated renal surface *per se* allows little or no urine to escape.

Later swellings may be due to secondary infections. A considerable and increasing well-defined swelling (colon pushed forward) with remission of acute symptoms and absence of inflammatory signs, would indicate the retroperitoneal accumulation of a well-walled-off collection of urine which is shut off from escape down the ureter; exploratory puncture (if deemed wise) will prove the condition.

It is obvious that we are not able to diagnosticate accurately the extent of many of these lesions. We know also that many such injuries, while not rapidly producing death, may do so eventually on account of the many complications that may arise. My feeling is that we should not hesitate in dubious cases to complete our diagnosis by an early exploratory lumbar incision which will also fill a useful and probably necessary therapeutic role. Not many years ago we thought ourselves competent to differentiate the several forms of appendicitis; few surgeons today care to take such a risk, preferring to replace doubt with certainty; and I believe that the varying possibilities for harm of a kidney lesion furnish a reasonable analogy.

In regard to prognosis, statistical data of large series of cases have been collected to show results both of the condition, and the value of the various forms of treatment, but it is doubtful if the older figures have much value today.

Suter,⁴ in 1905, found in a study of 701 subcutaneous injuries of the kidney: Total mortality, 18.6 per cent.; mortality of 131 treated by nephrectomy, 16.7 per cent.; mortality of 143 conservative operations, 14.6 per cent.; mortality of 427 treated expectantly, 20.6 per cent. If these figures are of any value at all, certainly an expectant treatment which has a mortality of over 20 per cent. does not make a very impressive showing. With modern technique, generalization of skilled operators, efficient means of combating shock, etc., to refrain from operation satisfied with a mortality of 20 per cent. cannot be accepted as progress. Watson showed in a series of 99 cases of operation in which the condition of the kidney called only for minor procedure there were only 7 deaths, the cause of death generally being found due to conditions independent of the operation proper (injury of the other kidney,

⁴ Beit. zur klin. Chirurgie, Band xlvii.

peritonitis). Watson has formulated the indication for treatment as follows:

Cases Suitable for Expectant Treatment: (1) The milder forms of the injury. (2) The cases in which there is reason to believe that both kidneys have been injured, the signs being external evidence of injury on both sides, tumor in both loins, and anuria. (3) Cases in which there are injuries of other parts of the body of such grave character as to make futile any operative treatment of the renal lesion.

Cases Demanding Operative Treatment: (1) All in which there is evidence of progressive hemorrhage, for example, increasing pallor, pulse of declining strength and increasing rapidity, sighing respiration, and, locally, a tumor in the loin which is increasing in size, or an increasing amount of free fluid in the peritoneal cavity in the cases complicated by intra-abdominal injuries. (2) Hematuria which persists for a long time, even though the quantity of blood is at no one time large; hematuria in which there is a large amount of blood, even though it has not lasted long; hematuria which recurs after having ceased; sudden cessation of a previously profuse hematuria, and, if there is no reason to believe that both kidneys are injured, absence of hematuria. (3) Anuria which continues for more than thirty-six or, at most, forty-eight hours, and if there is no reason to believe that both kidneys are injured. (4) Cases in which there is evidence of intra- or perirenal suppuration or of peritoneal infection.

My own feeling would be that we should refrain from immediate operation in: (1) All milder cases, presenting no one symptom of any severity, and giving a history of injury which is presumably of no great violence. (2) Cases of generalized injury with a very bad general condition and absence of urgent kidney symptoms.

For the latter class I would urge an exploratory operation with an appreciable increase of any or all symptoms at an early date. Operation in some form then is indicated for all milder cases that show a tendency to increase their symptoms and for all other cases, barring those falling in Class 2. My attitude in the borderline cases would be, when in doubt, to operate, believing by such a routine measure we will not let some seemingly mild case slip through our fingers. As regards the time of operation, in general one should operate as early as possible, but if the main symptom is not that of an increasing anemia (repeated examinations of the hemoglobin), one might well occasionally give the patient a few hours in which to pull himself together, though such a delay should not be entertained if we have associated intraperitoneal injuries calling for prompt relief.

Operative Treatment. As a rule, the incision should give an extra-peritoneal approach by the lumbar route. It is the most direct, avoids infecting the peritoneum, and does not require

handling and blocking off of protruding intestines. Moreover, it will provide the safe and efficient drainage demanded in most of these conditions. An anterior incision should be reserved for injuries which presumably involve the intraperitoneal organs; even in these cases a supplementary lumbar incision for drainage may be indicated, particularly if a nephrectomy is not performed.

Treatment of the Injured Kidney. Nephrectomy should be reserved for the cases in which the integrity of the kidney cannot be preserved, and it is obvious that hemorrhage cannot be effectually stopped or prevented otherwise, or the outflow of the urine into the ureter cannot be effectually restored. In the event of doubt arising regarding the integrity of the other kidney, nephrectomy may be deferred until sufficient information is obtained. Meanwhile, the injured kidney should be attended to, the peritoneum if torn should be sutured or packed, lacerations sewed if advisable, the pelvis drained, and the whole or part of the wound packed and drained efficiently. Where nephrectomy is not required, suture or packing with drainage will suffice. How much more efficient suture rather than packing a lacerated area will prove is to me an open question. I think not much time should be lost in performing it, and it should perhaps be reserved for cases in which packing may less efficiently check bleeding. The main indication is to provide free drainage which will minimize the disastrous secondary effects of injury and extravasation.

This paper is written to call attention to the fact that rupture of the kidney in children is probably commoner than generally estimated. That the lesion is frequently severe, consisting of a complete division of the kidney into unequal halves. That shock and other symptoms may be slight and out of proportion to the gravity of the lesion. That operative interference should be more freely employed and gives good results.

THE SO-CALLED "MIXED" TUMORS OF THE SALIVARY GLANDS.

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THE mixed tumors of the salivary glands were carefully reviewed by Wood in 1904. His article gives a detailed report of his observations on the pathology of 42 cases and contains a clear *resume* and

fairly complete bibliography of the pathologically significant literature to that date. His conclusions in brief are as follows:

"1. There is a group of extremely complicated tumors occurring in the facial region which contain elements from both epi- and mesoblast in most intricate relationship to each other.

"2. The complicated structure of the stroma, containing as it does elements such as embryonic connective tissue, cartilage, bone, fat, and lymphoid tissue, and very rarely striated muscle is explained most easily by the assumption of an embryonic misplacement of mesoblast.

"3. The structure of the parenchyma is so slightly characteristic in morphology that its epithelial nature in all cases can only be considered as probable; yet in about 24 per cent. of the tumors examined the presence of epithelium is undoubted. The form and relationships of the cells of the parenchyma do not furnish sufficient data to justify these cells in being regarded as of epithelial origin.

"4. The theory of early embryonic displacement of epiblastic tissue during the process of formation of the parotid and submaxillary gland and the branchial arches may account for many of the morphological peculiarities of the cells of these tumors, especially the lack of any typical features which we associate with epithelium. The same conditions may be seen in the epithelial cells of the congenital moles in which the epithelium is with difficulty distinguished from connective-tissue cells, owing to its close connection with the stroma of the tumors and its undifferentiated type.

"5. The mixed tumors of the salivary gland run a clinical course strikingly different from the sarcomas and carcinomas in that they are slow growing and generally benign. The regional lymph nodes are not invaded and recurrences are likely to remain local in a considerable proportion of the cases."

Since the publication of Wood's article an extensive literature has grown up. A bibliography thereof is appended. The following papers may be briefly noted as of pathological interest: Verhoeff reports 5 cases of tumors of the lacrymal gland and discusses the various theories of the formation of these tumors and of the mixed tumors of the salivary gland. His conclusions are as follows:

"The mixed tumors of the lacrymal and salivary gland (so-called endotheliomas) are essentially epiblastic in origin. The stroma of these tumors is not derived from mesoblastic cells misplaced from other structures, but is probably produced by an atypical development of cells which ordinarily would have gone to form part of the stroma of the normal gland. Owing to their situation the tumors of the lacrymal gland are not only dangerous to sight, but are more dangerous to life than those of the salivary gland and should be extirpated as soon as possible."

Keen observed one of the largest mixed tumors of the parotid reported, the specimen weighing seven pounds.

Ehrich reports his observations on the pathology of 33 tumors of the salivary gland. He gives a detailed report of the cases, both clinically and pathologically, and a lengthy discussion of the literature.

Martini, who has studied 6 cases, reviews the literature at great length and discusses the various hypotheses of origin of the tumors. He noted in his cases that in the peripheral parts of the tumors the stroma consisted of a more or less strongly developed framework of fibrous or reticular structure which was directly united with the capsule and that the same in advancing toward the centre of the tumors changed its structure, assuming the appearance of thick and tough or soft and loose connective tissue or a myxomatous or cartilaginous connective tissue. . . . No sharp limit existed between the various kinds of connective tissue. . . . The endotheliomatous formations were more luxuriant in those zones where the stroma had a fibrous structure. He concludes: "(1) The presence of fibrous connective tissue in the youngest parts of a tumor and of myxomatous and cartilaginous tissue in the oldest parts of the same indicate that these varieties of the connective tissue present the product of a metaplastic process of the fibrous stroma and not the product of processes developing at the cost of *germi-aberrantes* or other mesenchymal elements. (2) Besides the different phases of evolution of the neoplastic cells and their slow or rapid growth one observes the various phases of alteration and transformation of the stroma. . . . The question of the significance and origin of the myxomatous and cartilaginous tissue in the mixed tumors remains still undecided."

Martini was unable to identify the presence of true gland tissue in his mixed tumors. He asserts that the "acini" are without a limiting membrane and that the supposed epithelial cells are intimately related to the stroma. He thinks he can trace the origin of the tubules and cell formations from proliferated endothelium in the lymph vessels.

Massabuau reports on 4 mixed tumors of the parotid, 1 of the submaxillary gland and 1 of the velum palati. He discusses at length the literature and various theories of development, but finally concludes, "the theory which explains in a perfect manner the structure of these mixed tumors of the salivary gland is that which explains their development from ectomesodermic rests of the embryonic bud which was destined to the formation of the glands themselves. (1) It is the one important fact in the development of the mixed tumors on the border of glandular organs. (2) It explains the new formation of the flat epithelium as well as of the normal and edematous glandular epithelium. . . . (3) It explains perfectly the *intrication* of the two orders of endo-

thelial proliferation. . . . (4) There is no need of invoking, as in the endothelial theory, a cellular metaplasia for explaining the development of the polymorphous connective stroma of these tumors."

Speese reports his study of 9 cases, 8 of which were tumors of the parotid gland and 1 sublingual.

Fick reports a careful study of 2 cases, which he thinks do not support the hypothesis that tumors are endotheliomas.

Cordier reports in detail 1 case.

Von Hanseemann has recently studied one enchondroma of the parotid in which he thinks he can without doubt trace the development of the parts from lymphangioma. He says, "I consider in fact this tumor a lucky finding which makes it possible to advance the sureness of the endothelial nature of the so-called parotid enchondromas. That lymph angiomas are present in the parotid has been long established. That, up to this time, such characteristic stages as are present in the tumor in question were not found is because these tumors were only seldom studied in the initial stages."

Sertoli makes a careful study of 4 cases and assumes that though the tumors may be of endothelial nature this is not opposed to the theory of their development from *germi aberrantes*.

The object of the present paper is to place on record the results of the analytic study of 56 mixed tumors of the salivary glands, which have been removed at operation at St. Mary's Hospital (Mayo Clinic), from January 1, 1905 to April 10, 1911.

The following tables give the sex and age incidence of onset, duration, and period of operation of the cases of "mixed" tumors of the salivary glands which we have studied:

TABLE I.—Sex and Age Incidence at Onset of Symptoms.

Decades:	2d	3d	4th	5th	6th	7th	Total.
Cases, males	3	10	10	3	3	1	30
Cases, females	6	5	6	6	3	..	26
Total	9	15	16	10	6	1	56

TABLE II.—Time from Onset of Tumor to Date of Operation.

Time:	1	4	8	9	1	2	3	4	5	6	7	8	10	13	15	20	25	27	30	44	Total.
	mo.	mo.	mo.	mo.	yr.	yr.	yr.	yr.	yr.	yr.	yr.	yr.	yr.	yr.	yr.	yr.	yr.	yr.	yr.	yr.	
Cases, males	1	1	1	1	4	5	1	.	1	3	1	1	3	1	2	1	.	1	1	.	30
Cases, females	1	.	.	.	5	4	3	2	2	4	1	2	1	.	.	.	26
Total	2	1	1	1	9	9	4	2	3	7	2	3	3	1	2	1	1	1	1	1	56

TABLE III.—Sex and Age Incidence at Time of Operation.

Decades:	2d	3d	4th	5th	6th	7th	8th	Total.
Cases, males	2	5	8	8	3	3	1	30
Cases, females	3	4	7	5	4	3	..	26
Total	5	9	15	13	7	6	1	56

From these tables it will be seen that the sexes are almost equally divided, but with a slight preponderance of males. From Table I above it will be seen that the age at onset in more than two-thirds of the cases is under forty years, while in one-half the cases it falls between twenty and forty years. These figures agree, on the whole, with those of other observers. For example, of Wood's 42 tumors, 4 appeared in the first decade, 1 in the second, 13 in the third, 8 in the fourth, 9 in the fifth, 4 in the sixth, and 3 in the seventh. Thus almost two-thirds of his cases also began before the fortieth year. When the figures for Wood's series and ours are added, the percentages by decades at time of onset are approximately as follows: First decade, 4 per cent.; second decade, 10 per cent.; third decade, 28 per cent.; fourth decade, 24 per cent.; fifth decade, 19 per cent.; sixth decade, 10 per cent.; seventh decade, 4 per cent. These percentages are considerably advanced over those of Kaufmann and Küttner, who describe the majority of these growths as beginning in the second decade. Looked at broadly, the salient point of these figures is that 66 per cent. of the tumors began before forty years of age and 85 per cent. of them before fifty years of age.

Some interest attaches to the length of the period between the onset of the tumor and the time of surgical operation. As will be seen from Table II, this varies from one month to forty-four years, with a large preponderance of the cases running from one to ten years, and an average of six years and four months. The average of Wood's cases for the same period was eight years and nine months. When the figures for his 42 cases and our 57 cases are combined (total 99 cases) they give an average duration of symptoms prior to operation of seven years and four months. The obvious lesson from this is that these tumors do not cause sufficient inconvenience to the patients to make them seek operation early. In only 14 of our cases was there a history of pain. It is difficult to say, whether, if the patients were seen earlier, it would have a material effect on the final results of the operation, since, as will be noted later, the tumors which are carried longest without giving unpleasant symptoms are those which are apparently benign. The age at operation, as shown in Table III, indicates that the majority of these patients are in a favorable period of resistance.

Acute Parotitis. Certain observers have attempted to trace a relationship between mumps and "mixed" tumors of the salivary glands. Of the 21 of our patients with tumors of the parotid who could give a definite history concerning mumps, 14 (66 per cent.) were sure they had never had the disease. In other words, there seems to be no etiological relationship established by the statistics of mumps and "mixed" tumors of the parotid.

Location and Gross Appearance. Of our 56 tumors, 50 were in the parotid and 6 in the submaxillary glands. Thirty were on the right side and 26 were on the left side. Grossly, the tumors



FIG. 1.—Case XIII. Group 1. Dense fibrous tumor.



FIG. 2.—Case X. Group 2. Area showing cartilage.

may be divided into four groups: (1) Hard, fibrous masses with little cartilage and with little parenchyma (see Fig. 1); in this group were 15 cases. (2) Very hard tumors containing large cartil-

age masses (see Fig. 2); in this group were 17 cases. (3) Soft, more or less sarcoma-like tumors with relatively small amount of



FIG. 3.—Case XVIII. Group 3. Loose parenchyma in cords.



FIG. 4.—Case XXXV. Group 3. Parenchyma showing tubules.

fibrous connective tissue and a relative large amount of parenchyma cells (see Figs. 3 and 4); in this group were 20 tumors. (4) Tumors grossly resembling carcinoma; in this group were 4 tumors.

Histology; Stroma. Thirty-three of our cases showed marked increase of the fibrous connective tissue; 17 of these showed cartilage formation. In all of the cases in which the parenchymatous element was in marked preponderance the connective tissue appeared to be of distinct embryonic type. This connective-tissue type of embryonic cells was also present in some areas of the more fibrous tumors. In 35 of the cases a more or less distinctly myxomatous tissue was present (see Fig. 5). In many tumors was present a transparent, hyaline structure. It was noted that the cartilaginous and myxomatous elements were apt to be near the centre, that is, older portions of the tumors, rather than near the advancing borders where the simple fibrous connective tissue and parenchyma were greatly in predominance or constituted the whole of the tissue. This, of course, suggests a metaplastic origin of the cartilage, hyaline, and mucoid structures.

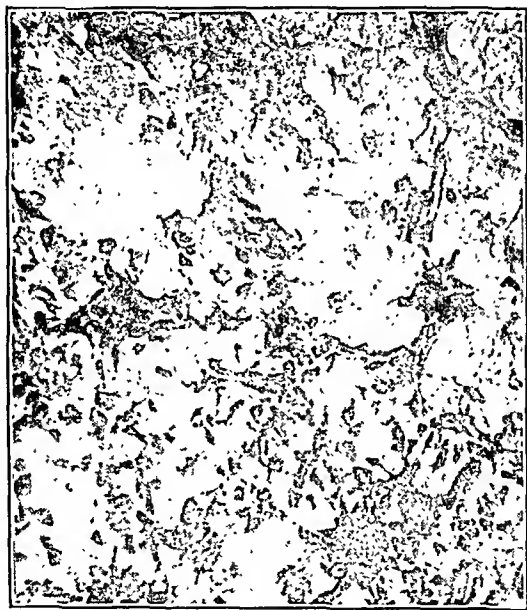


FIG. 5.—Case XVI. . Group 1. Myxomatous change

Bloodvessels. In 24 cases more or less endarteritis was present. These were about equally distributed throughout the four groups as above classified from their gross appearance. In these cases the proliferation within the vessels did not seem to us as sufficient in amount or of such a type as to suggest tumor formation within them. On the contrary, the changes appeared to be rather the result of chronic irritation.

Parenchyma. In Group 1, that is, the hard, fibrous tumors, the parenchyma cells are usually found in small, distorted groups, which are frequently interpreted as the result of endothelial pro-

liferation. The same is true in certain areas in Group 2, namely, the tumors with a marked cartilaginous element. Less rarely do such cell elements occur in the tumors of Group 3, those with loose, abundant parenchyma, and then only in small areas. On the other hand, in these parenchymatous tumors the cells of the advancing neoplasms are more frequently arranged in cords (see Fig. 3) or tubules (see Fig. 4) which strongly suggest the normal histology of the gland. A careful examination of the flattened and distorted cell groups, so frequently interpreted as "endotheliomas," leads one to the belief that they are either (1) adult epithelium which has been flattened and distorted by pressure, or (2) proliferating embryonic transitional mesothelium which has never attained



FIG. 6.—Case XV. Group 4. Mass of epithelium.

adult type. There is a direct relationship between the amount of parenchyma and the rate of development and malignancy of the tumors.

In many instances the variation in morphology in the parenchyma cells is so far retrogressive that it approaches the true spindle-celled sarcoma type. In some cases there is such a preponderance of cells of the aberrant, epithelial type (see Fig. 6) that one hesitates whether or not to diagnosticate such tumors as carcinomas. We have, however, included within our series only those cases of salivary gland tumors which show a newgrowth of two or more of the types of fibrous connective tissue, cartilage, sarcoma cells or adult epithelial cells.

All degrees of adhesion to and shrinkage away from the alveolar

walls by the lining parenchyma have been found. This point which has been made so much of by Volkmann we consider as having little diagnostic value.

Etiology. The origin and development of the so-called "mixed" tumors of the salivary glands must be considered in relation to the origin and development of other "mixed" tumors. These have recently received considerable study. Attention may be called to the articles by Stoerk and by the present writers attacking the Grawitzian hypothesis of the so-called renal "hyper-nephromas," and those by Ewing and Stoppato on the teratomas of the testicle.

There is, however, little to add to the discussion of the derivation of these tumors as given by Wood. Perhaps the matter of most interest related to their development is the growing belief of embryologists that the parotid gland takes its rise much earlier in the embryo than was formerly supposed. It now seems to be somewhat definitely settled that the *anlage* of the parotid appears about the fourth week instead of the eighth week of embryonic life as was formerly taught. At this period the mesoblastic tissues through which the gland bud forces itself are much less differentiated than they are in the eighth week. These facts are, therefore, in better accord with the hypothesis that the "mixed" tumors of the parotid are derived from areas of imperfectly developed mesoblastic tissue than was the former teaching of the later embryonic development of the parotid gland. So far as our personal observation goes, it would seem to us that the weight of evidence is in favor of the theory that these tumors are the result of proliferation of mesoblastic tissue perhaps displaced early in the embryonic development of the glands or which for some reason has failed to attain adult characteristics.

Results of Operation. Thirteen of our cases had been operated on elsewhere before they appeared at this clinic. These, therefore, represent cases of recurrence. Of the 42 cases which have been heard from since being operated on here, 9 have had a recurrence of the disease. Five of these were cases in which the neoplasm was of the loose, markedly sarcomatous type, and 4, cases in which the original growth was of the hard, fibrous type. Five of these 9 cases have died. Of these 5, 2 cases had tumors with a large epithelial element and in 3 the largest element of the tumors was of sarcoma type. All of these cases have died away from the clinic and no opportunities have been afforded to make postmortem examinations.

As has been pointed out by Judd, the recurrences are caused mostly by the difficulty of removing all portions of the tumor and yet preserving the fibers of the seventh nerve. When a tumor is already sarcomatous or carcinomatous at the time of operation the chances for recurrences are materially increased.

MIXED TUMORS OF PAROTID GLANDS.

Group, Case No.	Registered No.	Sex	Age.	Duration of symptoms.	Previous operation.	Date of our first operation.	Subsequent history.	Side affected.	Previous parotitis.	Pain.	Rate of tumor growth: Rapid = R, Slow = S.	Macroscopic type of tumor.	Vessels: increase = +, decrease = -; end-arteritis = E.	Stroma: increase = +, decrease = -; hyalin = H.	Cartilage.	Cell groups: alveoli = A; solid masses = SM.	Cells: cuboidal = C, flat = F; spindle = S, small round = SR.	Mitotic figures.	Myxomatous changes.	Calcification.
1	D. 2082	M	20	8 yr.	1905 Jan. 3	OK, 5 yr. 6 mo.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
2	G. 4541	M	44	8 yr.	Mar. 27	OK, 4 yr.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
3	G. 47584	M	50	1 yr.	May 10	O. K., 3 yr.	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
4	G. 2091	F	37	7 yr.	May 25	O. K., 6 yr.	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
5	J. 8124	F	44	1 yr.	July 10	Rec., 5 yr.	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
6	J. 3013	M	33	2 yr.	July 20	Died 1 yr. 3 mo.	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
7	S. 302	F	34	1 yr.	July 25	Rec., 2 yr.	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
8	Mrs. J. W. J. 1507	F	57	8 yr.	Mar. 7	O. K., 4 yr. 3 mo.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
9	J. 1507	F	47	5 yr.	June 23	O. K., 4 yr.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
10	Miss A. S. 1907	F	20	3 mo.	July 26	O. K., 4 yr.	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
11	Pl. Bk., 14	F	38	2 yr.	Mar. 18	O. K., 3 yr. 4 mo.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
12	P. 6022	M	50	2 yr.	April 10	O. K., 3 yr. 2 mo.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
13	Ho., 61	F	56	7 yr.	May 22	O. K., 3 yr.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
14	Gif., 1704	M	19	1 yr.	May 22	O. K., 3 yr.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
15	J. 2073	M	28	1 yr.	May 28	Rec. 1 yr. 6 mo.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
16	Dr. A. M. J. 17	F	37	2 yr.	June 10	Rec. 3 yr. 4 mo.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
17	Bk. or M16	F	30	2 yr.	June 11	O. K., 3 yr.	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
18	J. 2738	M	47	10 yr.	0 yr.	June 15	O. K., 3 yr.	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
19	J. 2830	M	31	12 yr.	July 15	Rec., 3 yr.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
20	Mfr. C. J. F. 19	M	37	10 yr.	Aug. 7	O. K., 3 yr.	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
21	A1712	M	70	30 yr.	Inf.	Sept. 24	Rec., 6 wk.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
22	A3042	F	20	1 yr.	Nov. 23	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
23	A5357	F	25	1 yr.	Op., 3 yr. 6 mo.	Jan. 11	O. K., 2 yr.	L	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
24	A7340	F	27	5 yr.	Rec., 2 yr.	Mar. 7	Rec., 2 yr.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
25	A1559	M	43	15 yr.	July 22	O. K., 2 yr.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—
26	A18330?	F	18	6 yr.	Sept. 10	O. K., 2 yr.	R	?	+	S	1	+	+	+	—	C, S, SR	—	—	—

27	A12357	F	34	2 yr.	July 27	?	L	+	+	S	2	E	+	+	SM	F, F	+	+
28	A5175	F	31	6 yr.	Jan. 6	Rec., 1 and 2 yr.	L	+	+	R	3	E	+	+	A, SM	C, F	+	+
29	A18358	M	61	4 mo.	Dec. 28	Died 1 mo. later	L	+	+	R	4	E	+	+	SM	C, F	+	+
30	A4689	M	38	7 yr.	Feb. 6	O. K., 1 yr. 6 mo.	R	+	+	S	2	E	+	+	A, SM	C, F	+	+
31	A22140	F	50	7 yr.	April 6	O. K., 1 yr. 2 mo.	L	+	+	S	3	E	+	+	A, A	SR, C	+	+
32	A21697	F	34	8 yr.	Mar. 27	Rec., 1 yr.	L	+	+	S	2	E	+	+	SM	F, S, SR	+	+
33	A22675	F	62	2 1/2 yr.	April 21	O. K., 3 yr. 4 mo.	R	+	+	S	3	E	+	+	A, SM	F, S, SR	+	+
34	A26098	F	24	6 yr.	Op., 3 yr. Rec., 6 mo.	Oct. 14	Rec., 6 yr. 2 mo.	L	+	+	R	3	E	+	+	SM	F, C	+	+
35	A31134	F	43	3 yr.	Nov. 13	O. K., 1 yr.	R	+	+	S	3	E	+	+	SM	F, S	+	+
36	A3898	M	27	3 yr.	Feb. 9	O. K., 4 mo.	R	+	+	S	3	E	+	+	SM	F, C	+	+
37	A34574	F	30	6 yr.	Feb. 25	O. K., 4 mo.	L	+	+	S	3	E	+	+	A, SM	F, C	+	+
38	A37071	F	54	4 1/2 yr.	April 3	O. K., 2 mo.	L	+	+	S	3	E	+	+	SM	F, S	+	+
39	A37735	M	71	1 yr.	10 mo. ago	June 19	Died 3 mo.	L	+	+	R	3	E	+	+	SM	S	+	+
40	A38746	F	62	25 yr.	25 yr. 20 yr.	June 14	Rec.	R	+	+	R	2	E	+	+	A, SM	F	+	+
41	A39230	M	55	20 yr.	June 23	O. K., 3 mo.	L	+	+	R	3	E	+	+	A, SM	F, C	+	+
42	A39803	M	57	27 yr.	July 8	L	+	+	S	3	E	+	+	A, SM	F, C	+	+
43	A40330	M	25	5 yr.	July 16	Rec. after 4 mo.	R	+	+	S	3	E	+	+	A, SM	C, SR	+	+
44	A14953	M	39	2 yr.	Aug. 22	R	+	+	S	2	E	+	+	A, A	C, F	+	+
45	A42737	F	42	2 yr.	Sept. 2	L	+	+	S	2	E	+	+	A, A	C, F	+	+
46	A28505	F	58	1 yr.	Oct. 1	R	+	+	S	2	E	+	+	A, A	C, F, SR	+	+
47	A44948	M	60	8 mo.	6 mo. ago	Oct. 25	L	+	+	R	3	E	+	+	A, SM	C, F, SR	+	+
48	A46670	M	41	13 yr.	2 rec.	Dec. 12	R	+	+	R	1	E	+	+	A, A	C, F, SR	+	+
49	A48731	F	24	4 yr.	Feb. 7	R	+	+	S	1	E	+	+	SM	C, SR	+	+
50	A51433	F	64	44 yr.	April 6	R	+	+	S	1	E	+	+	SM	C, F, C	+	+

MIXED TUMORS OF SUBMAXILLARY GLANDS.

1	P. 2463	M	39	6 yr.	1905	O. K., 5 yr. 2 mo.	L	+	+	S	2	E	+	+	SM	C, F, S	+	+
2	G. 5570	F	46	1 mo.	Apr. 8	O. K., 4 yr. 8 mo.	R	+	+	R	4	E	+	+	A, SM	C, F, S	+	+
3	I. 1255	M	61	9 mo.	1906	O. K., 4 yr.	L	+	+	R	1	E	+	+	SM	S, SR	+	+
4	M. 2552	M	16	6 yr.	Mar. 27	R and L	+	+	S	2	E	+	+	SM	C, S, SR	+	+
5	A21949	M	49	15 yr.	June 6	R	+	+	R	2	E	+	+	SM	C, S	+	+
6	A31575	M	40	1 mo.	1909	R	+	+	R	1	E	+	+	SM	C, S	+	+
					Mar. 31	R	+	+	R	2	E	+	+	SM	C, S	+	+
					Dec. 1	R	+	+	R	1	E	+	+	SM	C, S	+	+

Summary. 1. The present study covers 50 "mixed" tumors of the parotid and 6 "mixed" tumors of the submaxillary glands.

2. Most of the "mixed" tumors of the salivary glands arise in young adults.

3. Most of the tumors cause little inconvenience early and surgical relief is not sought until an average period of about seven years has passed.

4. Our cases show no etiological relationship between the tumors and acute parotitis.

5. The tumors which grossly are hard, consisting of fibrous connective tissue or cartilage are proliferating at their periphery only and are usually benign.

6. The tumors which grossly are soft, consisting largely of parenchyma of types varying from adult to embryonic are those among which are found the malignant tumors.

7. Connective-tissue and parenchymatous elements both tend to revert to embryonic type.

8. There is little evidence that these tumors arise from proliferating adult epithelium, or endothelium.

9. There is considerable evidence to support the theory that these tumors are mesotheliomas of embryonic origin.

10. After fairly complete operative removal few of the tumors recur.

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DUODENAL ALIMENTATION.¹

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WHEN Einhorn first described his method of duodenal alimentation about a year and a half ago, I realized its possibilities and began using it in certain selected cases. After a considerable

¹ Read before the New York Academy of Medicine, February 15, 1912.

experience I regard duodenal feeding as a distinct mark of progress in the treatment of those conditions where rest for the stomach is indicated. The principal field for its usefulness lies, of course, in the treatment of certain gastric and duodenal ulcers, but its scope can be legitimately enlarged by including certain other conditions, as will be shown later.

For those who are not acquainted with the duodenal tube, I will briefly outline the technique of its use. The tube is swallowed by the patient at bedtime, with the aid of water. When the first mark on the tube is at the teeth the bucket on the end is entering the stomach. The second mark indicates the distance from the mouth to the pylorus. During the night the capsule, provided there is no obstruction, will usually have passed the pylorus and the third mark on the tube should be at the teeth, indicating that the end of the tube is *in situ*, well down the duodenum.

Before starting the feeding it is well to make sure that the tube is really *in situ*. This is done in several ways. Gentle traction will develop a slight resistance if the tube is in the duodenum. Aspiration through the tube will often recover golden-yellow duodenal juice and not gastric secretion. Lastly, and most certain, if the patient be given some liquid to drink by mouth and aspiration is immediately performed it will not be returned through the tube as would be the case if the latter were coiled up in the stomach.

When certain that the tube is in place we can proceed with the feeding. The food which has been found most satisfactory is a mixture of milk, sugar of milk, and raw egg. The amount given at a feeding should be small at first, 100 c.c. every two hours from 7 A.M. to 9 P.M., increased until 280 or 300 c.c. are taken at each feeding, if possible. When the patient is taking 280 c.c. of milk, one egg, and one tablespoonful of sugar of milk at each feeding he is receiving approximately 2840 calories for the total eight feedings in the twenty-four hours. As the average individual while in bed requires under 2000 calories to maintain his nitrogenous equilibrium, it can be seen that there is a liberal amount in excess for the purpose of building up the patient.

Einhorn uses the glass syringe to administer the food, and by means of a feeding table which fits over the glass of nourishment, is able to fill the syringe from the glass and by a manipulation of petcocks force the contents into the duodenal tube without disconnecting.

In treating my first 2 patients I thought it would be advantageous to employ a method like that of Murphy for giving salt solution per rectum, and so I have made use of gravity from a pint irrigating jar, connecting its tube to the duodenal tube by a glass connection and setting the rubber petcock so that the nourishment enters the duodenum slowly, about twenty-five minutes being required for the larger feedings.

Duodenal alimentation is not, as a rule, suitable for use in the home unless a nurse who has had some experience with it is in constant attendance. There are a number of points which must be adhered to rigidly or untoward happenings will occur. As a rule, if the patient's relatives are entrusted with giving the feedings some mistake will result in the patient being made uncomfortable or the tube being blocked up so as to necessitate its withdrawal in order to clean it.

The food must be administered at body temperature. Food normally entering the duodenum from the stomach is at body temperature, and so the former is not accustomed to shocks of too high or too low temperature, and resents such insults by distressing symptoms of shock, cold perspiration, flatulence, and distress, and perhaps even syncope. The mixture should be heated gradually, preferably in water, and should not be made too hot lest it become thick and lumpy from cooking of the egg. After heating it should be strained. This will help in preventing the tube from becoming occluded.

The food should be allowed to enter the duodenum slowly. Too rapid administration will cause flatulence and often the same symptoms as variations in temperature.

At the termination of each feeding a syringe of water at body temperature should be injected; then the petcock closed; the syringe filled with air; the petcock again opened and the air injected, after which the petcock should again be closed before the syringe is disconnected. This keeps the tube cleared and clean. The management of the petcock is not trivial, as it might seem, and if, say, the petcock was not turned off when the syringe is removed, some of the food would likely rush back into the bucket and lower tube and be converted by the trypsin into a cheesy lump, defying removal until the tube is removed and cleaned. It is because of the importance of these details that one who has had experience should superintend the feedings.

Duodenal feeding is only to be chosen for certain cases. Certain ulcers with severe symptoms, which would heretofore have been treated at the beginning by rectal feeding for some days, may at once be put upon duodenal feeding. Again, in an ulcer which has not healed under a thorough course of medical treatment we should try duodenal alimentation before resorting to surgery. By so doing we can eliminate several of the factors which tend to prevent ulcer from healing, that is, the presence of acid in the stomach, irritation of food in the stomach, stretching of the stomach, and peristalsis. At the same time the body secures sufficient nourishment.

This method of treatment will not cure all cases of ulcer, and some may have to be operated upon later; but in all in whom I have tried it, the general condition of the patients has been decidedly

improved, so as to render them better surgical risks. The following synopses of 2 cases which later came to operation show this point.

Miss M. T. D., aged thirty-four years, had symptoms for nine years, complaining of pain and tenderness in the left epigastrium, coming on from two to three hours after meals, and severe headaches. The pain was decidedly aggravated whenever she was much on her feet. There was no nausea or vomiting. Her gall-bladder was distinctly palpable and slightly tender, but not distended. The right kidney was palpable to the second degree. A spot of some tenderness was found on deep pressure, one-half inch below and one inch to the left of the ensiform. Splashing sound extended over the entire epigastrium to the navel. There was slight hypersecretion and an acidity of 64. The diagnosis was not clear for several weeks, as occult blood was absent from the stools, but this appeared later, at which time the thread test also became positive. After she had been on the rest treatment for two weeks and her symptoms were worse, if anything, it was thought best, in consideration of the probable long duration of the ulcer, to put her on duodenal feeding at once. She improved greatly on the treatment, but after a time her symptoms reappeared and a gastro-enterostomy was performed, an ulcer being found in both the stomach and duodenum.

Another case, that of Mrs. M., is interesting, as at operation later on, scars of two healed ulcers were discovered demonstrating that the duodenal feeding had been successful, but that other ulcers had developed after a year of health. She came to me with symptoms of recurrence of an ulcer, which had apparently been healed by medical treatment the year before. Her weight was only ninety-eight pounds. She complained of a severe epigastric pain and tenderness. Occult blood was present in considerable amounts and the thread test was positive. Operation was thought advisable, but it was decided to first try duodenal alimentation, as her general condition was very poor. The tube was left *in situ* for eighteen days, during which period her symptoms entirely disappeared. Her weight progressively improved, and in several months it reached 116 pounds, a gain of 18 pounds. Later the symptoms of ulcer recurred, and Dr. Howard A. Kelly found at operation several scars in the stomach from the ulcers healed by the former treatments and an open duodenal ulcer which was producing the symptoms at the time.

Ulcers at the pylorus, producing obstruction, may be treated with duodenal alimentation, provided the duodenal tube can be passed into the gut; but if the pylorospasm persists they then demand gastro-enterostomy. Duodenal alimentation or other forms of medical treatment should not be given too long a trial in an unhealing ulcer at the pylorus, even if not producing obstruction, because of the danger of malignancy. But in other ulcers this method of

treatment should be instituted in nearly all cases after ordinary medical means have failed to produce a cure, and will often bring about happy results. I have never had a complete failure in any ulcer case in which I have used the tube, that is, one in which no improvement whatever was noted. Many complete cures have resulted, as far as can be determined, and the remainder were greatly improved.

The cases which were not of long duration have almost without exception done well, as in the following:

Mrs. H. C. M. had symptoms of two months' duration when she first consulted me. She complained of a burning pain in the stomach and pyrosis about three hours after meals, and in the early morning, relieved for a time by food, soda, or belching. Ulcer was not diagnosticated at first since examination failed to show tender spots, and the stool was negative for occult blood. The right kidney was palpable to the first degree and splashing sound was obtained over the whole upper abdomen as far down as the lower border of the navel. Free acid was 34 and total acid 48. Under a general reconstructive treatment she at first improved somewhat, but became decidedly worse while on her vacation, so that three months after her first examination she returned with exaggerated symptoms and a positive thread test. Duodenal feeding resulted in complete relief from her symptoms, and a negative thread test, which has persisted.

Mrs. O. came to me in the spring of 1911, shortly before I left town on my vacation. Her family history was good. She had been delicate as a child, and had always been troubled more or less with digestive disturbances. During the previous two years she had been having attacks of sharp pain in her stomach, which at first would come on several hours after her evening meals. She also complained of distress in the region of the sigmoid, more or less constant in the earlier hours of the day, which to a great extent passed off after bowel actions. There was a decided tendency to a relaxed condition of her bowels. She was troubled with a continuous dull headache. Chest organs were normal. Her abdominal walls were relaxed. Splashing sound of stomach reached from ensiform to one inch below navel. A good deal of tenderness was elicited by pressure over her sigmoid, but at no other point. Her hemoglobin was 75 per cent.; leukocytes, 10,400, with a polymorphonuclear count of 75 per cent. The urine showed a very faint trace of albumin. The feces showed a good digestion and no occult blood. Stomach digestion was good, free HCl being present with an acidity of 56 and no occult blood. Because of a tendency to diarrhea, the distress in her sigmoid in the early part of the day, the tenderness to palpation in that region, the blood picture, and her progressive loss of strength and some weight, I feared lest a beginning malignant change was occurring. However, as

she and I were just leaving town for the summer nothing further could be done other than to regulate her diet, etc. In the early fall upon my return she again came to see me, and I found her general condition unchanged. Her chloroanemia was slightly more pronounced but the leukocytes and polymorphonuclear count were both quite normal. There was less sigmoid distress although the bowels were acting from three to eight times each day, the feces being always loose and mushy. However, the epigastric pains were now more pronounced and occurred from one to three hours after every meal, being worse after the heavier and more complex meals. Her bowels began to act from one-half to two hours after every meal, remarkably coincident with the onset of her pains. A point of marked tenderness was elicited below the right costal border, the thread test was positive, and occult blood was present when on a meat-free diet. She was put upon the conventional rest treatment for cure of ulcer, and kept there for several weeks, but without any marked amelioration in her symptoms for any length of time. Every attempt to increase her diet brought all her former symptoms. At the end of this time I put her upon duodenal feedings in the manner described in the previous cases. She kept the duodenal tube *in situ* for thirty-two days continuously without having it removed once, and without the slightest untoward symptoms. From the end of the first forty-eight hours she was free from all her subjective symptoms. At the end of the third week her bowel actions were reduced to one normal stool daily, and at the end of the fourth week the feces were free from occult blood. The tenderness had disappeared from the epigastrium, although there was still a sensitive area over the sigmoid. At the present time she has been on nearly a normal diet and has been about the house for some weeks; her blood is normal, and she has regained her normal weight and strength.

Such cases as these I could multiply many times over in my experience to illustrate the great reliability and usefulness of duodenal feeding in similar cases.

Einhorn in some cases of gastric ulcer, recommends the local application of healing agents by painting argyrol in nearly insoluble form on the tube at the point where it rests against the ulcer. I have not had a large experience with this method, but I have administered various drugs through the tube for other conditions arising during the course of duodenal feeding. In the diarrheas which so often accompany duodenal ulcer, prompt relief is often secured by 1 grain of argyrol in 1 ounce of warm starch water given through the tube. Flatulence caused by the milk not agreeing perfectly can often be controlled by the addition of 30 drops of glycerin to the feeding. If flatulence still persists, 5 drops of ichthyol in a little water through the tube is generally followed

by good results. Where the stool shows deficiency of bile we have often seen the yellow bile color reappear promptly upon the administration of 1 or 2 minims of dilute hydrochloric acid in 1 ounce of water through the duodenal tube.

Apart from the treatment of ulcers, duodenal alimentation may be employed with benefit in some other cases. I have secured happy results in the treatment of duodenal catarrh by using a long duodenal tube. Warm Carlsbad water can also be administered through the tube at the same time.

In one case of cancer of the stomach in which there was marked dysphagia and a sensation of closing up of the throat, so that partial starvation was resulting from the patients failing to take sufficient nourishment, I was, after two attempts, able to get the tube to pass the pylorus, and the patient was afforded considerable relief, and his strength improved for a time, by feeding through it.

There is another class of cases in which results have been most striking—namely, cases of visceroptosis of marked degree, with ischochymia, where it seems as if the stomach is incapable of emptying itself and passing along sufficient of the forced feeding to increase weight and restore the general tone. This to my mind is a strong indication for duodenal alimentation.

The stomach is given a rest, and at the same time food can be introduced into the body in sufficient quantities to cause increase in weight and improvement in muscle tone. A striking example of this is the case of Mrs. D. T. D., who was emaciated, and had a marked visceroptosis, with ischochymia. The lower border of her stomach was three fingers' breadth below the navel. She took the tube for twenty-one days and again for fifteen days. She did well from the start, and the gain was spectacular. Altogether she has gained 34 pounds, and it seems to be permanent. Previous to the duodenal feeding she had made but little progress.

Miss R. A. had marked enteroptosis for seven years, which had been treated without benefit by many physicians. She was much emaciated and a pitiable object. A long rest cure with forced feeding helped but little, but after a course of duodenal feeding she has made marked progress, and has gained 40 pounds.

I consider that duodenal feeding constitutes a mark of great progress in medicine, filling a long-felt want, a method of resting the stomach, and at the same time affording the economy abundant nourishment. In those cases in which it is indicated the results are most gratifying.

TYPHOIDAL HEMIPLEGIA WITH REPORT OF THREE CLINICAL CASES AND ONE WITH NECROPSY.

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HEMIPLEGIA following or occurring during typhoid fever is a comparatively rare complication, and any cases of this character are well worth reporting. It has been mentioned as early as 1860 by Gubler,¹ but since then, to my knowledge, there have been few cases published.

Among the more recent literature on this subject the paper of Smithies² takes up and classifies the symptoms, prevalence, age, time of occurrence, etc., in considerable detail.

In compiling the cases already published, with those described in this paper, several points are of interest.

The male sex was more often affected (70 per cent.) than the female (30 per cent.) in the 40 cases in which the sex was defined.

Where the side involved was tabulated, left hemiplegia occurred in 19 (44 per cent.) and right hemiplegia in 24 (56 per cent.).

In 28 cases of right side involvement aphasia was noticed in 23 (82 per cent.), while it is mentioned in only 3 (18 per cent.) of the 17 left hemiplegics.

The complication occurred before the age of ten years in 9 instances (24 per cent.), before twenty in 10 cases (26 per cent.), and in 19 (50 per cent.) before the age of thirty years.

Of those cases in which the time of onset was given, 10 (24 per cent.) occurred in the first and second week, 8 (20 per cent.) during the third week, 4 (10 per cent.) during the fourth, 15 (40 per cent.) during convalescence, and 2 (5 per cent.) so late after the attack as to render the dependence of the condition upon typhoid rather doubtful.

Athetosis was reported by Curschmann,³ Osler,⁴ and Barrett,⁵ and is also present in my first case.

Visual defects have not occurred, with the exception of a left-sided amaurosis and nerve atrophy in an interesting case described by Benedikt.⁶ Here there was also stuttering with the left-sided hemiplegia. Stuttering was also one of the symptoms of my first case. In Pigott's⁷ case the pupils were dilated, the right larger than the left and less reactive to light than the left,

¹ Arch. Gén. d. Méd., 1860.

² Jour. Amer. Med. Assoc., August 3, 1907, vol. xlix, No. 5. In this paper a very complete list of literature up to 1907 is given.

³ Nothnagel's Handbuch, Band iii, I Teil.

⁴ Johns Hopkins Hosp. Rep., 1899 to 1900.

⁵ Report of Michigan State Asylum for Insane.

⁶ Elektrotherapie, 1868.

⁷ Maryland Med. Jour., 1909, lii.

also deviation of eyes to left. This was a left hemiplegia. A case of left hemiplegia reported by Parisot,⁸ which ran a course of a few days, showed inequality of the pupils and strabismus. In Case IV there was deviation of the eyes toward the right with left-sided hemiplegia.

Sensory changes in most instances were absent or so slight as to be doubtful in value. Such changes were present in the case of Raschofsky's⁹ and Case I of this paper.

An interesting case, more of a meningitic type, is described by Laure¹⁰ in which, in addition to the typical signs of a meningitis, there occurred an aphasia with loss of ability to write, but no paralysis.

The hemiplegia occurring in typhoid does not differ materially from one following any other cause, and should therefore be readily diagnosticated. In some cases the onset may be acute, with convulsions or delirium or a rapidly developing coma or general restlessness with increase in the temperature, while in others it may be very gradual, extending over a period of hours or days or even weeks (Nothnagel), and in some instances reported there was no positiveness concerning the exact time of the occurrence of the paralysis.

This variety of onset is dependent to some extent upon the reactive or resistant condition of the patients' nervous system, but much more upon the character of the pathological lesion causing the condition. Thus, in the early cases where there is perhaps more likely to be a hemorrhage or an embolus, the onset is acute and there may be convulsions and coma. When, however, the symptoms are the result of a toxemia, there would more probably be a delirious condition of some duration, with temperature elevation in cases of an encephalitic character. In the convalescent stage there would be, more likely, a gradual onset, such as might occur in thrombosis, this lesion being in all probability the one which most frequently occurs during this stage of the disease.

A higher percentage of cases has been reported as occurring during the stage of convalescence, and this is due in all probability to the generally weakened condition of the patient at this period, the sluggishness of the circulation, and the condition of the vessels and the blood, tending to aid in the formation of thrombi in the cerebral vessels just as they do in the better known thrombotic processes elsewhere in the body.

The prevalence of this complication in the male sex is dependent upon a greater percentage of typhoid occurring in males, and also upon the fact that the male, through excessive venery and abuse of alcohol and tobacco, is more subject to such vascular changes as predispose to a thrombotic process.

⁸ Rev. méd. de l'Est. Nancy, 1909, xli.

⁹ Wien. med. Woch. 1911, No. 39

¹⁰ Rev. Neur., Paris, 1908, xvi.

The question of athetosis and choreic movements present in Case I, also reported by Curschmann, Osler, and Barrett, is of considerable interest as it is caused by involvement of some vessel other than the one so frequently affected. It might be due to an affection of the meningeal vessels, causing irritation, or of the vessel or vessels supplying the lenticular and thalamic regions.

The pathological condition most frequently occurring in these hemiplegics is in all probability a thrombosis, this being due in great part to the causes mentioned earlier in my paper. Thrombi were found in the Sylvian fissure branch of the middle cerebral artery by Dankin,¹¹ Hawkins,¹² Osler,¹³ Barrett,¹⁴ and in my fourth case. Embolic softening would in many cases be difficult to distinguish from thrombosis—cases of this nature were published by Curschmann¹⁵ and Hruska.¹⁶

Parisot¹⁷ reported a case in which the internal carotid was thrombosed at its entrance to the skull, and as a result the central part of the right hemisphere, the external capsule, and basal ganglion were totally destroyed, leaving only a shell of the cortex intact. Curschmann's case had a diffuse hemorrhage in the lenticular area.

Some of the hemiplegias, particularly the more transient and rapidly healing ones, may be caused by a toxemia affecting the cerebral cells, and this interpretation would more readily explain the great percentage of cases having a complete or almost complete recovery. Barié and Lian¹⁸ referred to the probability of such an origin in their case.

Encephalitis may also be the basis of some of the cases, as in the one reported by Raschofsky.¹⁹ Here the increase of the temperature at the time of the onset of the symptoms with restlessness and the recedence of the fever with the return to normal, led the author to consider an encephalitis as the cause.

The prognosis is dependent to a great degree upon the character of the lesion present. In those cases of toxic or encephalitic origin the recovery may be almost complete. Where a hemorrhage or thrombosis is the basis of the condition, the change would be much slower and less complete. As a rule, the leg regains its power and function much earlier than the arm and hand. Aphasia, if present, may improve, but very seldom clears up entirely (Smithies). Treatment is largely symptomatic with the necessity of avoiding the use of any drugs or measures that might lead to hemorrhage. The late stages require the usual massage with general tonic treatments.

¹¹ *Lancet*, April 23, 1892.

¹² *Loc. cit.*

¹³ *Loc. cit.*

¹⁴ *Loc. cit.*

¹⁵ *Loc. cit.*

¹⁶ *Loc. cit.*

¹² *Clin. Soc. Trans.*, 1889.

¹⁴ *Loc. cit.*

¹⁶ *Präg. med. Woch.*, 1901, Nos. 41 and 42.

¹⁸ *Bull. et. Mem. de la Soc. d. Hôp. de Paris*, 1907.

Papers have been written on cerebral and meningeal complications of typhoid by Du Castel,²⁰ Cabanes,²¹ Barthelemy et Durbin,²² Starkiewicz,²³ Diller,²⁴ Antony and Dofter,²⁵ and Laignell-Levas-tine.²⁶ Cases have been reported by Lesieur,²⁷ and Tondi,²⁸ also an atypical case of post-typhoid thrombosis by Pasteur.²⁹ I regret that I have been unable to obtain the records of any of these.

I am greatly indebted to Dr. William G. Spiller for the privilege of reporting the following cases, 2 of which were examined by me at the University and Philadelphia Hospitals, and a microscopical examination made in the third.

CASE I.—E. K., aged twenty-two years. Admitted to the Philadelphia Hospital December 2, 1908.

Family history negative as regards possible affections of the nervous system.

Patient was well up to the age of six, when he developed typhoid fever. During the attack of typhoid fever he was confined to bed for three weeks. He remembers that he was wildly delirious during this illness, and wanted to jump out of the window. He also claims to have been unconscious during part of his illness, but does not know the duration of the unconsciousness. About two months after onset, and a week or so after beginning to improve, upon attempting to get up one morning he found that he could not use his left leg and arm, but does not know whether or not he could move his arm and leg while in bed. He was not able to walk for some time. His speech was affected so that people said he talked "tongue-tied," and he had trouble in swallowing. There were at no time any other symptoms of head involvement such as headache, vomiting, etc.

The athetoid movements of toes and fingers were present as long as he can remember, but he does not think they anteceded the attack. His left foot felt heavier and colder than the right, and he dragged it in walking.

Examination upon admission. Left arm was flexed and adducted, and was continuously and rhythmically flexed and extended. Fingers were flexed and athetoid movements were constant. The biceps was markedly contracted and prominent, and various muscles of the forearm could be seen contracting rhythmically. The left arm with a great deal of exertion could be raised to the level of the shoulder. The forearm could be flexed and extended slightly, and with very little strength. Pronation and supination were not possible. The handgrasp was very weak, as were the

²⁰ Gaz. des Hôp. de Paris, 1910, lxxxiii.

²² Gaz. med. de Nantes, 1906, xxiv.

²¹ Jour. Amer. Med. Assoc., May 27, 1905.

²³ Arch. d. méd. et pharm. Paris, 1905, xlv.

²⁴ Bull. et mem. des Hôp. de Paris, 1907, xxiv, No. 30.

²⁵ Bull. de la Soc. méd. des Hôp. de Lyons, 1907, vi.

²⁶ Arch. Middlesex Hospital, London, 1909, xvi.

²¹ Bull. med. del. Algeriei, 1908, xix.

²³ Gaz. lek Warszawa, 1906, xxiv.

²⁸ Napoli, 1909, xxiv.

individual finger movements. The entire upper extremity was very spastic and resistant to passive movements; no atrophy. The left lower extremity showed retained power of flexing the leg on the abdomen, but this was greatly weaker than on the right. The leg could be flexed and extended at the knee, but no movement was possible with the toes, nor could the foot be elevated. The left foot was held in a partially flexed and adducted position, and continuous athetoid movements of the toes were present. Reflexes were markedly increased with ankle clonus and a Babinski strongly positive. Spasticity with resistance to passive movement was excessive. The leg was dragged in a spastic manner, but not swung in a circle, as it so often is in hemiplegics. Hypalgesia and hypesthesia were found over the entire left side, but no change in the temperature and position senses. Some slight asteriognosis was present in the left hand. There was no involvement of rectum and bladder.

Examination March, 1910. There remains distinct foot drop and atrophy of tibialis anticus and the peroneal group. The calf muscles are contracted. The thigh muscles are still somewhat weaker than the right. At present the athetoid movements occur in the fingers and in the arm when the patient attempts to resist passive movements. There is some slight impairment of the lower facial movements.

CASE II.—W. P. (No. 4218). Aged sixteen years. Male. Admitted to the University of Pennsylvania Dispensary December 11, 1905.

The patient was perfectly well up to four years ago, at which time he had a severe attack of typhoid. During this illness he had a left-sided hemiplegia, this having occurred while he was still in bed and running a temperature. The leg and arm were both affected; he could not move his fingers properly, nor the left side of the face. The patient said he could not talk for two days, although this might have been due solely to the involvement of the tongue and face. The eyes and ears seemed to be all right.

Examination on admission showed the left arm somewhat contracted and atrophied, with the reflexes increased, and the hands cyanotic and cold. No sensory changes were present. The power in the shoulder muscles was fair, but impaired. The patient had a distinctly spastic hemiplegic gait. All reflexes were increased with positive Babinski and some atrophy of the entire leg. There were no sensory changes.

CASE III.—Mrs. L. G., aged thirty-two years, white. Admitted to the University Dispensary September, 1910.

The patient always had good health until four years ago (1906), when she had typhoid fever, and was in bed twenty-one weeks. During her illness her right arm and right leg would frequently drop over the side of the bed and would have to be lifted back.

They were manipulated by the nurse, and when handled were always stiff and sore. When the patient got out of bed she experienced no especial difficulty in walking or standing, although she had to use a cane. The arm and hand were used only with great difficulty, and their original strength has never returned.

The right upper limb has never recovered in strength or size. She uses it awkwardly, and is forced to make more fine movements with the left hand. When she walks the right foot is dragged along the ground.

Examination. At rest the right side of the face shows some drooping in the lower half. Actively this is less marked, but still present. She winks the right eye less than left; wrinkles brow well. The tongue deviates to the right on protrusion. Ocular movements are good; reflexes normal. The upper extremities show marked weakness in all movements of the right arm, with all reflexes considerably increased. The entire limb is smaller than the left. There are fibrillary twitchings, but no sensory anomalies. The left arm is normal. There is no vesical or rectal disorder.

Lower extremities. Gait is unilaterally spastic. The patient drags the right foot. Individual movements are fairly well performed with right leg, very well with left. The whole right lower limb is distinctly smaller than the left. There are no fibrillary twitchings or sensory changes.

Reflexes. On the right the patellar tendon and Achilles tendon reflexes are greatly exaggerated. Ankle clonus is not demonstrable, probably on account of spastic contracture of Achilles tendon. The Babinski sign is present. On the left the reflexes are somewhat increased but not abnormal, and no Babinski.

Other than a slight thickness of speech during the first period of the attack, there was no disturbance of speech.

CASE IV.—B. C., male, colored, aged twenty-four years. Admitted to Dr. B. F. Stahl's ward in the Philadelphia General Hospital (and examined by Dr. Spiller), January 6, 1906. Died January 10, 1906.

During the course of typhoid fever the patient sat up in bed and fell out toward the right, striking first upon his buttocks. He was put back to bed and Dr. Spiller, upon examining him, found a left-sided hemiplegia with deviation of the eyes away from the paralyzed side. The fall was regarded as due to cerebral hemorrhage or a thrombosis of the middle cerebral artery. The patient died five days later. Necropsy showed congestion of liver, spleen, and lungs, and typhoid ulceration of the ileum; apparently typhoid in the third week.

At necropsy a thrombus was found in the artery of the right Sylvian fissure and microscopically the areas supplied by this artery were found to have undergone softening with the presence of a great many fatty bodies or cells and cellular debris.

A STUDY OF THE BLOOD OF PATIENTS WITH PULMONARY TUBERCULOSIS UNDERGOING SANATORIUM AND TUBERCULIN TREATMENT.

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THE following study of the blood was made at the Adirondack Cottage Sanitarium between the years 1904 and 1911. Some of the work was for a time included in the ordinary routine work of the institution and other parts of it were taken up as separate investigations. Dr. Lupton, who was engaged upon the work at first, to our great regret, died before it was completed. The observations have been made as carefully as possible, and our work has been influenced by the excellent monograph of Kjer-Peterson, to which reference is made later.

ERYTHROCYTES.

Number per Cubic Millimeter. The number of red blood cells per cubic millimeter appears from a study of 273 cases to be slightly above normal. The figures for these cases were:

Incipient.					Moderately Advanced.			
	Cases.	Average.	Median.	Mode.	Cases.	Average.	Median.	Mode.
Male .	. 77	5,630,000	5,500,000	5,000,000	63	5,710,000	5,500,000	5,000,000
Female	. 68	5,277,000	5,000,000	4,500,000	65	5,316,000	5,000,000	5,000,000

These cases when charted in the form of a frequency curve show for the incipient cases that the mode¹ for women is 4,500,000, for men slightly over 5,000,000. For the moderately advanced cases the mode for both men and women appears to be 5,000,000. The curves in both instances show a rather sharp rise and a slightly less rapid fall. The median and the mode differ slightly, the former being slightly higher than the latter.

Relation to Pulse Rate. The patients were divided into groups, accordingly as the erythrocytes ranged from 4,000,000 to 4,499,000

¹ The mean is the average value (or "average"); the median the middle-most value when the values are ranged in order of magnitude; the mode is the value which occurs most frequently. When the median and the mode coincide the mean gives an exact idea of the frequency relation; when they are widely separated the mean is of far less and often of uncertain value.

and so on up to 7,500,000, and in each group was placed the number of patients with a pulse rate of 80 to 89, 90 to 99, and so on to 120. The maximum for seven days on admission gave the average. The following conclusion was reached, namely, that the number of erythrocytes in incipient tuberculosis in males is smaller than in moderately advanced tuberculosis for pulse rates below 100. In women the same holds for any pulse rate. There were 128 men and 118 women studied.

Relation to Color Index and Color of Mucous Membranes. In calculating the color index 5,000,000 is used as a standard in both incipient and moderately advanced cases. If for women 4,500,000 is used as the standard the color index will be 10 per cent. higher. The mucous membranes were classified as follows: good color, slightly anemic, anemic, and slightly cyanotic, according to the appearance at examination on arrival. No relation was found to exist in 237 cases.

Relation to Hemoglobin and Color of Mucous Membranes. The cases were divided according to the number of erythrocytes into groups of 1,000,000 from 4,000,000 up to 7,999,000. They were arranged in these groups according to the percentage of hemoglobin, 60 to 69 per cent., 70 to 79 per cent., and so on. The color of the mucous membranes was classified as above. Nothing was learned in a study of 130 incipient and 107 moderately advanced cases.

Relation to Extent of Physical Signs. The following cases were studied:

	Turban.	I.	II.	III.
Males		85	28	5
Females		81	32	6

The results were tabulated, but showed little variation between the two groups.

HEMOGLOBIN.

The hemoglobin was measured on admission by the Talquist scale and occasionally with the von Fleischl instrument in 272 patients with the following results:

	Incipient.		Moderately Advanced.	
	Cases.	Average per cent. Hb.	Cases	Average per cent. Hb.
Males	77	92	62	91
Females	68	89	65	88

The results in the incipient and moderately advanced stages for males and females as well as the totals in each group were charted. The mode in every case but one was 90 per cent., the moderately advanced male group having 95 per cent. as the mode.

LEUKOCYTES.

Number per Cubic Millimeter. In all 275 cases were studied, with the following results:

Incipient.					Moderately Advanced.				
	Cases.	Average.	Mean.	Mode.	Cases.	Average.	Mean.	Mode.	
Male . . .	68	10,074	9000	8500	63	10,443	10,000	10,000	
Female . . .	69	9,425	8000	7000	65	10,642	10,000	8,000	

When a frequency curve for these cases is charted it is seen that for incipients the mode is between 7000 and 8000, with a sharp rise from 4000 and a more gradual decline to 16,000. The males and females each exhibit a less marked mode at 8000 to 9000 and 7000 respectively. For the moderately advanced cases the mode lies between 8000 to 10,000, with a sharp rise from 5000 and a gradual decline to 20,000. The males and females each exhibit a fairly well-marked mode at 10,000 and 8000 respectively. These figures all relate to counts made on admission, as the counts made on discharge are too few for any inductions to be drawn, but would seem to indicate that the curves are much flatter.

Relation to Duration of Disease. The cases were tabulated according to the length of illness, 0 to 5 months, 6 to 11 months, and so on to 120 months. The leukocytes were grouped into thousands from 5000 up to 21,000, and an attempt made to see what effect duration of disease had upon the number of leukocytes. There seemed to be no relation in 107 cases.

Relation to Weight. Incipient and moderately advanced cases, male and female, were arranged in groups, accordingly as their weights were above or below standard, allowing ten pounds to each group. The cases in each group were arranged also according to the thousands of their leukocytes, 5000 to 21,000. Digestion was unimpaired and general condition good for all cases. Nothing was learned from this study of 168 cases.

Relation to Tubercle Bacilli in Sputum. The cases were arranged accordingly as tubercle bacilli were present (1) previous to admission, (2) at admission, (3) during residence, and grouped according to the number of their leukocytes, 5000 to 21,000. There was apparently no relation in 169 cases.

Relation to Condition on Admission and on Discharge. A single leukocyte count of each patient was taken on admission and on discharge. The condition of each case was charted accordingly as the disease was apparently cured, arrested, or failed, and also whether tubercle bacilli were present or absent. The temperature was normal in all cases. No information was gained from 169 cases.

Relation to Temperature. The cases were divided according to the number of leukocytes into six groups above and below 10,000, and the number of cases in each group classified as incipient or moderately advanced. The leukocytes taken at other times of the day in this study were grouped separately from the 8 A.M. counts. No relation was found to exist in 63 afebrile and 36 febrile cases. There were no cases with vomica.

Differential Count. In a study of 60 cases the percentage of the polymorphonuclears varied inversely with the percentage of the mononuclears, and was lowest in the incipient, higher in the moderately advanced, and highest in the far-advanced. The eosinophiles followed the same rule as the mononuclears.

	No. of cases.	Poly- morpho- nuclears.	Mono- nuclears.	Lympho- cytes.	Large mono- nuclears.	Transi- tional.	Eosino- philes.	Mast cells.
Incipient	16	64.9	33.0	28.6	2.0	2.4	2.0	0.1
Moderately advanced	32	69.3	29.6	24.6	2.8	2.2	1.0	0.1
Far advanced . .	13	81.4	18.0	14.1	1.3	2.6	.5	0.04

Tuberculin. In order to determine accurately the effect of tuberculin upon the number of leukocytes, we have calculated the mean error in the number of leukocytes in several instances. The method that we have followed is that adopted by Kjer-Peterson in his interesting work upon the numerical relation of the leukocytes in pulmonary tuberculosis. While Kjer-Peterson calculated the mean error from different specimens taken at the same time from the same man, we calculated the mean error from ten counts of leukocytes in the same pipette. We also calculated the mean errors on twenty different estimations of leukocytes, and found these to be in 5 cases, 3 per cent. of the number; in 11 cases, 4 per cent. of the number; in 2 cases, 5 per cent. of the number; in 2 cases, 5 per cent. of the number. The lowest mean errors in percentages were found in the largest number of leukocytes and the highest mean errors in percentages were found in the smallest number of leukocytes. The number of leukocytes on which the mean errors were calculated was between 3400 and 10,780. Using the formula of Kjer-Peterson we find that the mean error in the observation of a single

count is $Me = \sqrt{\frac{(O_1 - O)^2 + (O_2 - O)^2 + \dots + (O_{10} - O)^2}{9}}$. The

mean error of the mean of the ten observations or counts is

$$\sqrt{\frac{Me^2}{10}} = \frac{Me}{\sqrt{10}}.$$

The calculation was made as follows:

Observation count O_n	Deviation from mean $O_n - O$	Squares of deviation ($O_n - O$) ²
34	-1	1
33	-2	4
36	+1	1
25	-1	100
36	+1	1
42	+7	49
34	-1	1
37	+2	4
37	+2	4
36	+1	1
Total 350		166

$$\text{Mean } (O) = 35.$$

Me = mean error.

$$\text{Me}^2 = \frac{166}{9}.$$

$$\text{Me} = \sqrt{\frac{166}{9}} = 4.298.$$

Now 4.298 is 12 per cent. of 35, consequently the mean error in these observations was 12 per cent., which is much higher than Kjer-Peterson's (8 per cent.).

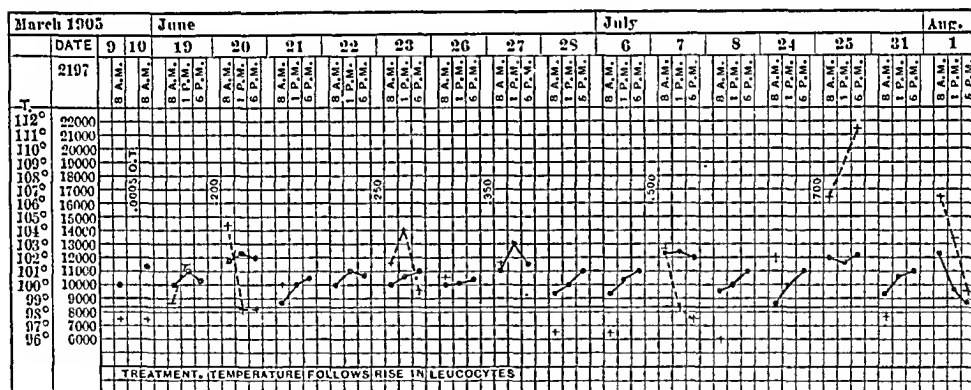


CHART 1.—Tuberculin treatment with O. T. Female, aged twenty-one years. Essential increase of leukocytes only after 700 mg. Lines with dots represent temperature; lines with crosses, leukocyte counts.

As Kjer-Peterson's studies of the number of leukocytes in the blood of women would seem to indicate that the number of leukocytes is not constant from day to day at any time of the day, varying from 3000 to 12,000, our observations have been confined to leukocytes in the blood of men, for the number of leukocytes in the blood of healthy men was found to be constant early in the morning, immediately upon awakening. The morning specimens were taken after bathing and dressing, at 8 A.M., before breakfast.

In 14 instances where specimens were taken first in bed and again after bathing and dressing in the morning, the difference between the two counts was not larger than the unavoidable error in observation in 12 instances. In 2 cases where the number of leukocytes was smaller after the bath the differences are respectively 18 per cent. and 17 per cent. However, the differences on the whole may not be larger than the differences caused by errors in observations and an unavoidable small inconsistency in the number of leukocytes in the blood taken in bed on different days, early in the morning. It would seem to appear, therefore, that it did not make any considerable difference in the number of leukocytes whether the counts were taken before or after bathing and dressing in the morning.

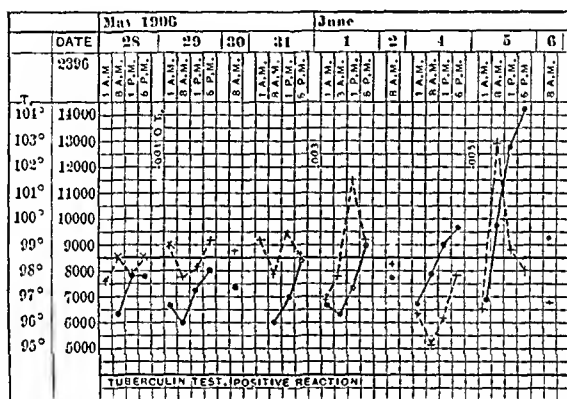


CHART 2.—Positive tuberculin test. Male, aged thirty years. Symptoms suggesting pulmonary tuberculosis. Essential increase of leukocytes after 5 mg. Lines with dots represent temperature; lines with crosses, leukocytes.

Tuberculin Treatment. The forms of tuberculin employed in the study were Koch's Old Tuberculin and the Bacillary Emulsion in varying doses up to 1000 mgs. of O. T. and 5 mgs. of B. E. The specimens of blood were taken at 8 A.M. after bathing and dressing, 1 P.M. and 6 P.M. before meals, and continued for many days during the course of treatment. In other cases, specimens were taken for five or six days in each month, at the same hours, and continued two to four months. We came to the conclusion from this study that there is no difference between O. T. and B. E. in their effects upon the leukocytes; that all doses may markedly increase the number of leukocytes; that there is little or no suggestion of leukopenia unless it comes shortly after the injection of tuberculin; that for a considerable increase in the dose there appears a considerable increase in the number of leukocytes corresponding to the increase in temperature, and that there may occur a rise in temperature without an increase in the number of leukocytes, and *vice versa* an increase in the number of leukocytes without a

rise of temperature. These studies were made after doses of tuberculin given at 8 to 9 P.M. When tuberculin is given at other times of the day it has not seemed possible to draw the same conclusions from our studies of the leukocytes. These observations were based on a study of 22 cases.

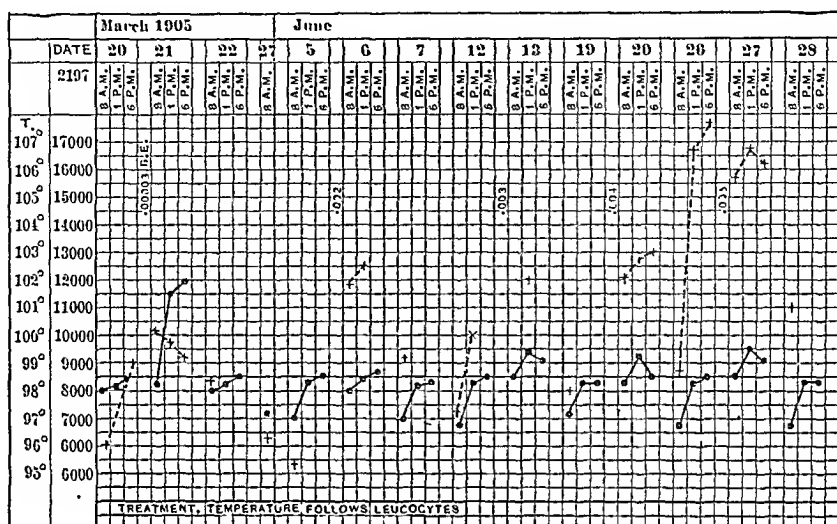


CHART 3.—Tuberculin treatment with B. E. Male, aged twenty-two years. Essential increase of leukocytes after last two doses of tuberculin. Lines with dots represent temperature; lines with crosses, leukocyte counts.

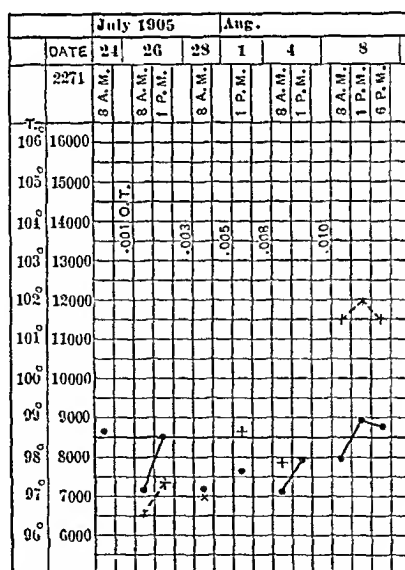


CHART 4.—Negative tuberculin test. Male, aged thirty-one years. Pulmonary abscess. Essential increase of leukocytes following 10 mg. of tuberculin. Lines with dots and crosses have the same significance as in preceding charts.

The Tuberculin Test. The tuberculin used was Koch's Old Tuberculin in doses of 0.5 to 10 mgs., given subcutaneously at

8 P.M., and specimens were taken at 1 A.M., 8 A.M. and 6 P.M. during the course of the test. The temperature was also taken at these hours. In order to determine whether there was a leukopenia following the dose and whether the temperature preceded or followed the rise in leukocytes when the patient reacted, tuberculin was given to another series of test cases at 8.30 A.M. and specimens were taken daily at 8, 10.30, 11.30 A.M., and 12.30, 1.30, 6 P.M. until reaction occurred. Specimens of blood were taken at the same hours on the day preceding the injection. It appears in this study that a reaction to tuberculin is almost always accompanied by a temperature. This followed in all these cases. During the period of reaction there is always an essential increase in the number of leukocytes when accompanied by a considerable increase in temperature; that the increase in leukocytes and temperature is usually closely connected; that the increase in leukocytes begin four to five hours after injection, and is closely followed by the rise in temperature. There was no evidence of a leukopenia observed in any of these cases. The rise of leukocytes is generally followed by a decrease in the number of leukocytes during the day after the first dose which causes an increase. In case of a repetition of the same dose or a slight increase of the dose the increase of the number of leukocytes corresponding to a considerable increase in the temperature appeared to be smaller and extended over a longer time. The counts taken at 1 A.M., four to five hours after injection, showed neither a leukocytosis nor a leukopenia. There were 27 cases studied.

NEUTROPHILIC BLOOD PICTURE OF ARNETH.

In 1904 Dr. Joseph Arneth endeavored to draw certain diagnostic and prognostic conclusions from hematological findings in pulmonary tuberculosis. His method depends upon an analysis of the nuclei of the neutrophile leukocytes, which constitute the bulk of the human white blood cells. He employed the usual dry smear with Ehrlich's triacid stain and divided the leukocytes into five classes according to the number of nuclei to a cell. His classification is arbitrary and somewhat complicated, and for a further description the reader is referred to his monograph.²

His original method was followed in a few cases, but it proved too laborious, and the subdivision of each class, accordingly as the nucleus was round, moderately indented, or deeply indented, was discarded, and we simply made divisions into five classes according to the number of nuclei to the cell.

Hastings' and Wright's stains were used and 200 cells counted.

² Die Neutrophilen weissen Blutkörperchen bei Infektionskrankheiten, Jena, 1904.

Date	Hour	1	2	3	4	5	0	10	20	30	40	50	60	70	80	90	100
8-1-08	8-AM	20	42	30	8	0											
8-2-08	"	18	51	24	7	0											
8-3-08	"	18	42	33	6	1											
8-4-08	"	31	44	20	5	0											
8-5-08	"	37	45	14	4	0											
8-6-08	"	22	45	27	6	0											
8-7-08	"	20	47	33	0	0											
8-8-08	"	38	43	12	7	0											
8-9-08	"	24	53	19	4	0											
8-10-08	"	17	44	31	8	0											
8-11-08	"	21	52	24	3	0											
8-12-08	"	13	49	28	4	0											
8-13-08	"	14	53	26	7	0											
8-14-08	"	34	42	22	2	0											
8-15-08	"	11	46	34	7	2											
8-16-08	"	9	47	39	5	0											
8-17-08	"	22	48	26	3	0											
8-18-08	"	24	55	18	3	0											
8-19-08	"	12	52	31	5	0											
8-20-08	"	13	48	33	6	0											
8-21-08	"	12	62	23	3	0											
8-22-08	"	7	55	30	7	1											
8-23-08	"	8	51	31	9	1											
8-24-08	"	19	46	32	2	1											
8-25-08	"	18	45	34	3	0											
8-26-08	"	26	56	18	0	0											
8-27-08	"	14	52	30	3	1											
8-28-08	"	22	47	22	6	1											
8-29-08	"	15	47	33	5	0											
8-30-08	"	17	50	24	2	1											
8-31-08	"	18	54	26	2	0											
10-8-08	"	21	52	15	11	1											

Table showing variation of the Arneth counts in an incipient case of tuberculosis.

Date	Hour	Leucocyte	Arneths	Count	1	2	3	4	5	0	10	20	30	40	50	60	70	80	90	100
2-8-08	8-AM	6800	49	41	9	1	0	0												
"	10-30 "	6300	53	38	9	0	0	0												
"	11-30 "	6000	49	41	10	0	0	0												
"	12-30PM	7800	50	46	3	1	0	0												
"	1-30 "	6400	55	44	1	0	0	0												
"	6- "	8400	42	47	10	1	0	0												
2-9-08	8-AM	6800	44	43	11	2	0	0												
"	10-30 "	6533	47	36	12	4	1	0												
"	11-30 "	9000	56	37	7	0	0	0												
"	12-30PM	8900	47	40	13	0	0	0												
"	1-30 "	9200	53	35	12	0	0	0												
"	6- "	10300	52	36	11	1	0	0												
2-10-08	8-AM	8200	41	42	15	2	0	0												
"	10-30 "	7200	50	44	6	0	0	0												
"	11-30 "	9133	48	43	9	0	0	0												
"	12-30PM	8266	48	44	8	0	0	0												
"	6- "	8133	48	38	12	2	0	0												
2-13-08	8-AM	8600	56	39	5	0	0	0												
"	10-30 "	7500	52	39	7	2	0	0												
"	11-30 "	7333	45	41	13	1	0	0												
"	12-30PM	6600	50	45	5	0	0	0												
"	1-30 "	4000	48	44	8	0	0	0												
"	6- "	5333	49	41	10	0	0	0												
2-14-08	8-AM	6333	48	36	16	0	0	0												
"	10-30 "	6133	48	43	9	0	0	0												
"	11-30 "	5425	43	44	11	2	0	0												
"	12-30PM	6400	43	49	6	2	0	0												
"	1-30 "	10900	52	38	8	2	0	0												
"	6- "	10750	48	36	14	2	0	0												
2-15-08	8-AM	7800	55	34	11	0	0	0												
"	10-30 "	8000	50	39	9	2	0	0												
"	11-30 "	7266	48	41	9	2	0	0												
"	12-30PM	6400	54	42	4	0	0	0												
"	1-30 "	5550	53	36	10	1	0	0												
"	6- "	6400	58	39	3	0	0	0												

Prob. Advanced T₂

Table showing effects of tuberculin on the total leukocyte and Arneth count of a moderately advanced case of tuberculosis.

In the tuberculin treated cases smears were made at 8 A.M. daily for one week, and in 2 cases daily for one month. In the tuberculin test cases, smears were taken six times daily, at 8, 10.30, 11.30 A.M., 12.30, 1.30, 6 P.M., until the patient reacted. From a study of 50 cases the following conclusions appear probable:

1. The nuclear picture is of no practical value in determining the dose of tuberculin for therapeutic purposes. In 2 cases which were followed daily for one month the blood curve showed no definite relation to the dose, and at no time made any appreciable deviation to the left or to the right.

2. In the course of the subcutaneous tuberculin test the blood picture is apparently not influenced until the stage of reaction occurs, when there may be a slight shifting to the left. This was not constant in all our cases.

3. In tuberculosis with extension of the infectious process there is a marked and permanent deviation of the blood picture to the left, indicating a grave prognosis.

BLOOD PRESSURE.

The instruments used were the Erlanger and Jancway sphygmomanometers, with a cuff 12 to 15 cm. wide. The blood pressure of all patients was taken a day or two after their arrival at the Sanitarium. A great number, however, had been in the mountains some weeks before being admitted. All patients were at rest, flat on their backs, on a couch, for at least five to fifteen minutes before the observation was made. Three to five records were taken, and if the variation did not exceed 4 mm. of mercury the average was entered as the blood pressure. The diastolic records are not as numerous as the systolic, owing to some imperfection developing in the Erlanger machine before our work was completed.³ The blood pressure of many of the same patients was taken again at discharge, which occurred some six months after their admission. At an altitude of 1600 feet we found the blood pressure to be:

Incipient.				
	Cases.	Average.	Median.	Mode.
Male	63	127 mm.	128 mm.	122 and 133 mm.
Female	75	121 mm.	118 mm.	112 and 128 mm.

As there are two modes the mean or average does not give us in this series of cases the true systolic level and consequently the systolic pressure lies between 120 to 125 and 130 to 135 mm. for males and between 110 to 115 and 125 to 130 mm. for females.

³ Owing to an imperfection in the Erlanger instrument the diastolic pressure was taken only in 84 patients. In 32 incipient cases it was found to be: males 86 mm., females 82 mm. In the moderately advanced cases: males, 85 mm., females 82 mm.

Moderately advanced.

	Cases.	Average.	Median.	Mode.
Male	118	126 mm.	125 mm.	125 mm.
Female	73	121 mm.	120 mm.	120 mm.

In this series of cases as the median and mode coincide the mean or average value gives us an exact idea of the true systolic pressure.

In the tuberculin treated cases (25) no appreciable effect was noted even after the largest doses (800 to 1000 mg. of tuberculin) had been given. The blood pressure of these cases was taken morning and evening and continued twice daily for two or three weeks. There were 329 cases studied.

TREATMENT OF ACNE WITH STOCK AND AUTOGENOUS ACNE BACILLUS VACCINE.

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VACCINE treatment in pustular dermatoses has now been in fairly extensive use for some time and varying results have been reported. By far the greater number, however, have been cases treated by vaccine of the two varieties of the staphylococcus, namely the albus and aureus.

It is now practically a recognized fact that cases of furunculosis and sycosis are cured much more rapidly by vaccine treatment than by any of the older procedures. Especially is this true in those resistant, long-standing cases of furunculosis, in which the disease is readily checked by a few injections of a stock vaccine, and a lasting immunity is produced by a continuation of the treatment.

In sycosis barbæ vaccine is of most benefit in clearing up those deep, indurated, nodular masses in which the infection has extended down into the subcutaneous tissues and the course of the treatment is much shortened by combining injections with the usual lotions and ointments.

The results obtained by the use of staphylococcus vaccine in acne vulgaris were not as successful as in the other pustular conditions. In the chronic cases some improvement resulted but the disease soon recurred, while in the acute cases where the outbreak consisted only of comedones and small superficial pustules, the results were practically negative. The present method of using a combination of an acne and staphylococcus vaccine has proved

much more successful in that it combats both of the infecting agents at once.

From results obtained, as well as from reports by Fleming, Gilchrist, Engman and others, there is no doubt that the acne bacillus plays a large part in the infective processes of acne, but that it is the primary cause of the disease and produces the hyperkeratosis of the outlets of the ducts and the hypertrophy and loss of function of the glands themselves is not accepted by all observers. Though the fact that the bacillus can be found in smears from all cases of acne and plays an equal, if not a greater, part than the staphylococcus is well recognized. For like the staphylococcus the acne bacillus can be found in the skin of individuals who are not, nor ever have been sufferers from the disease, in fact, it can be demonstrated in almost pure culture from the plugs expressed from the follicles along the inner border of the ala of the nose whenever an oily seborrheic condition is present.

The acne vaccine used in the following series of cases was prepared in the Cornell Laboratory of Clinical Pathology after the method published in the *Journal of Cutaneous Diseases*, February, 1911. The organism is grown on 2 per cent. glucose agar slants under anaërobic conditions, transplants being taken from the original growths whenever pure cultures were not obtained.

As regards technique it will be found much simpler not to combine the emulsions, but to use them from separate bottles, as in this manner the strength of the dosage can be easily regulated, the desired amount of the acne vaccine being drawn up into the barrel of the syringe and then the staphylococcus vaccine added to it and the whole quantity given in one injection.

The following reports are taken from some 50 cases of acne, most of them being well advanced and showing indurated and pustular lesions. Some of them are from private practice, the rest from Dr. Elliot's clinic in the Cornell Dispensary.

About one-third were treated by staphylococcic vaccine alone, of the remainder some were treated by autogenous vaccine, while for the rest a polyvalent stock emulsion was used made up from cultures obtained from the first series. In all cases smears were taken from the lesions and stained with Gram's stain to determine the presence or absence of the acne bacillus. In every case they were present, although in varying numbers. The constitutional treatment was simple and consisted of the correction of any digestive disturbance and regulation of the bowels, while locally a mild antiseptic lotion was employed to prevent a surface spreading of the infection.

The injections were begun with a dosage of 3,000,000 acne bacilli and 150,000,000 staphylococci, the same amounts being practically continued throughout the course of treatment, in no case a larger amount than 5,000,000 acne and 250,000,000 staphylo-

cocci being reached. The frequency averaged about one injection every five days. Abscesses and the larger pustules were wiped over with alcohol and incised before treatment was begun and the comedones were removed as thoroughly as possible, the processes being repeated if they recurred.

The autogenous and stock vaccine cases were treated as nearly alike as possible in order to make a comparison of the results obtained and the cases in both series were selected from the more severe, long-standing infections.

Between the results obtained in the two series little remained to choose, in fact the most brilliant success of all was a young woman suffering from a very widespread, pustular acne of four years' duration, who had received the polyvalent stock vaccine. All the patients showed marked improvement but some of them were lost trace of toward the end of the treatment, and have not been seen since. One patient who had been under autogenous vaccine stopped treatment when the condition showed only improvement and obtained employment somewhere in the south where he was able to be out of doors a good deal, but the improvement in general health completed the cure begun by the vaccine and he has remained free from lesions ever since. The immunity in the case of the young woman does not seem to have been so lasting, for her work was in a factory and the hygienic surroundings were not so good. At the time the course of treatment was stopped her face was entirely free from anything resembling an acne lesion. She remained away three months and then returned, four or five small superficial pustules having appeared on her forehead, one injection of the same vaccine was given, and she reported that the lesions promptly healed; the recurrence was, however, repeated in about two months, when she returned with a worse outbreak, but complaining of some menstrual disturbance which was corrected and a couple of injections of vaccine given. After that she remained in good condition for five or six months when a very slight outbreak occurred yielding easily to the vaccine. Since then she has apparently remained free from all lesions.

Another patient who was on stock vaccine, has shown himself most resistant to treatment. The case was one of long standing, and when first seen the condition had gone on to an extensive abscess formation on one side of the face. These abscesses were incised at the beginning of treatment, and at first good progress was made and a partial immunity established, but it was easily broken down and the patient is still under treatment. Although there is considerable improvement over the original condition the result is far from satisfactory. The failure is undoubtedly due to the poor condition of the general health, for antedating the acne invasion there was a tuberculous joint infection and wasting of the muscles of one leg which probably keeps his power of resistance below par.

In considering the use of the acne vaccine treatment several facts appear evident. First, that the results obtained with the polyvalent acne stock were fully as satisfactory as those obtained with an autogenous vaccine, also that much more depended on a careful oversight of the case, from the clinical standpoint, regulation of the amount and frequency of dosage and general hygienic care of patients, than on the fact that the vaccines were autogenous. This, of course, is of great advantage in the employment of the injection treatment, for the acne bacillus is at best a slow grower and requires considerable time and care.

Another fact observed is that old emulsions produce a more rapid immunity with less danger of local reaction or anaphylaxis than those freshly prepared. Any emulsion carefully prepared keeps indefinitely if care is taken to prevent contamination. This fact has also been observed in vaccine injections against typhoid, in which it has been shown that an old emulsion produces slight if any, constitutional reaction, as compared with fresh cultures.

A FATAL CASE OF TETANY WITH AUTOPSY FINDINGS SHOWING HEMORRHAGES IN THE PARA- THYROID GLANDS.

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It is an acknowledged fact that tetany occurring after an operation for the removal of goitre is to be attributed to the removal of the parathyroid glands along with the thyroid gland, and that tetany of children is due to disease of the parathyroid glands.

Whether non-operative or spontaneous tetany occurring in adults is due to disease of the parathyroid glands or not is a question which is not yet settled. Indeed, as yet we have only insufficient data for deciding this question, as only few cases of fatal tetany in adults with postmortem findings have been recorded.

It has been our good fortune to observe a case of tetany in an adult in which the clinical course and postmortem findings seem to leave no doubt as to the diagnosis.

The parathyroid glands, which were discovered in 1880 by Sandstroem, were forgotten for ten years and again brought to our attention by the French physiologist Glay in 1891. The vital importance of the parathyroid glands is very generally recognized.

These glands are found on each side of the thyroid gland and sometimes embedded in the same. The number and position of these little glands show great individual variation. They are more numerous in children than in adults, and are bean-shaped, flat, and slightly translucent, of a yellow-brown color, and never lobulated. Oftentimes it is hard to distinguish them from fat tissue. Microscopically they consist of epithelial cells. Hence the name "epithelial bodies" given them by Kohn.¹

The cell masses are arranged in lobules or cell chains, between which a connective-tissue stroma runs which is less developed in younger individuals than in older ones. The bloodvessels are embedded in this stroma. The parenchyma consists of two different kinds of cells: The first are large polygonal and sharply outlined cells (cell type I), the protoplasm of which is colorless or slightly stained with eosin. Between these cells we find a deeper stained intercellular substance. The second type of cells are rich in chromatin (cell type II). They are indistinct in outline, and their scanty protoplasm is stained more or less with eosin. These cells are in some places closely packed together, giving the impression of being free nuclei. Koenigstein² has demonstrated on serial section that both types of cells are identical, and are different forms of the same cell, the differentiation having been produced by functional activity.

Petersen³ demonstrated with methyl-green pyronin stain that cell type I is a cell resting, while cell type II represents the cell in functional activity. The epithelial cells in young individuals contain much glycogen, and later fat drops. A few colloid drops may be found.

The colloid production found in the thyroid gland is not found in the parathyroid glands. In older individuals the glands are infiltrated with many large interstitial fat cells, which develop from the perivascular connective tissue.

The physiological function of the parathyroid glands became known to us only in the last few years. After overcoming many difficulties, Glay, who made the first experiments on rabbits, showed that the animals died of tetany after total extirpation of the thyroid glands with all the parathyroid glands. On extirpation of the thyroid gland without the parathyroid glands death did not occur. Glay believed that the parathyroid glands can perform the function of the thyroid gland, but on account of the irregular results from his experiments he could not give a clear idea of the function of the parathyroid glands.

Mousson took up Glay's experiments and criticised the same. He experimented on dogs, and reached the conclusion that the extirpation of the thyroid gland without the parathyroid glands

¹ (Collective references.) *Ergebn. d. Anat. Entwicklungsgesch.*, 1899, ix.

² *Wien. klin. Woch.*, 1906.

³ *Virchow's Arch.*, clxxiv, 1903.

does not cause tetany, but causes a chronic cachectic condition which the animal outlives. The extirpation of the parathyroid glands alone cause tetany, with fatal result.

This strict dualism of Mousson has been confirmed by a number of investigators: Vassale,⁴ Genrali, Walbum, Pineless,⁵ Erdheim,⁶ Hagenbach, Iselin, and others. Therefore, two different diseases may be distinguished: tetany parathyreopriva and cachexia thyreopriva. The term tetany thyreopriva is misleading, and is only a collective name for undifferentiated diseases. Without going into details of further experiments on animals, we may compare these with our clinical experience with human beings. We know that after thyroidectomy on human beings, tetany is observed, and it is believed that this is due to the removal of the parathyroid glands. The experimental experience on animals has demonstrated the same.

Erdheim was the first to throw light on the subject of operative tetany after thyroidectomy. He examined in serial sections the throat organs of two individuals dying after thyroidectomy, and could not find any trace of the parathyroid glands. The remaining portion of the thyroid was sufficient, it seemed, to protect the individual from cachexia thyreopriva. The result of Erdheim's investigation is in accord with animal experiments. Since surgeons have learned to avoid removal of all the parathyroid glands, tetany is very rare after thyroidectomy. Absolute proof as to the different functions of the parathyroid glands and the thyroid gland is seen in cases of so-called athyroidismus, or complete congenital defect of the thyroid. Here we have the typical picture of cretinism. In the cases which came to autopsy the parathyroid glands were found, but there was no trace of the thyroid gland. Experimental experience and the clinical observations are in harmony, and all argument against the functional activity of the parathyroid glands can now be disregarded.

We now approach the important and, to us, the most interesting question of the relationship of idiopathic, infantile, and adult tetany.

Erdheim was the first to discover hemorrhages in the parathyroid glands in cases of infantile tetany.

Yanase⁷ was the first to study this subject extensively, which he did from the cases in Escherich's clinic. He examined the parathyroid glands of 89 children coming to autopsy without any

⁴ Rivista experim. di freniatr., 1897; Arch. ital. de Biol., 1898; Münch. med. Woch., 1906, Nr. 33.

⁵ Sitzungsber d. Kais. Akad. d. Wiss. in Wien, 1903, Abt. iv; Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1904; Arb. a. d. Wien, Neurol. Inst., Nr. 16; Arch. f. klin. Med., lxxxv, 1906.

⁶ Wien. klin. Woch., 1901, Nr. 41; Zeit. f. Heilk., Abt. f. path. Anat., 1904; Mitt. a. d. Grenzgeb., 1906, xvi; Ziegler's Beitr., 1903, xxxiii; Sitzungsber. d. Wien, Akad. d. Wiss., 1907, Abt. iii (mathemat.-naturwissensch.).

⁷ Jahrb. f. Kinderheilk., lxxvii, 1908.

selection, ranging from birth to the fifteenth year. He found hemorrhages or remains of them in 33 children. In all, he examined 104 parathyroid glands and found 71 with hemorrhages. Therefore, hemorrhages in parathyroid glands are of frequent occurrence.

Yanase made systematic investigations of the electrical irritability in sick children, and at death he examined the parathyroid glands in 50 cases which came to autopsy; 30 of these showed a normal electrical irritability. At autopsy of these 30 cases the parathyroid glands were found normal, and no hemorrhages were found. In contrast, he found increased anodal electrical irritability in 22 children; and in 12 (55 per cent.) of these, hemorrhages were found in the parathyroid glands. Of 9 children under one year of age hemorrhages were found in each case. In the other 13 all of whom were older than one year, only 3 showed remnants of hemorrhages. Yanase came to the conclusion that in the remaining 10, hemorrhages had occurred which could not be found at the time of autopsy.

The latest investigations of Haberfeld⁸ has thrown some light on such cases of infantile tetany where no hemorrhages were found at autopsy. He found in these cases more or less marked atrophy, with or without remnants of hemorrhages, such as pigment or cyst formation. His thorough histological examination of these parathyroid glands has shown that hemorrhages not only destroy the histological structure, but also inhibit the development of the parathyroid glands and lead to a hypoplasia.

The reason that no symptoms of tetany were observed at the time of hemorrhage which generally occurs at time of birth is explained by Escherich,⁹ that the central nervous system of the newborn is insensitive to tetany toxin. The susceptibility to tetany begins about the third month. This theory seems to be supported by Quest,¹⁰ who found that the brain of the fetus contains the greatest amount of calcium, which decreases with the age of the child, and the irritability of the brain is increased with the decrease of calcium.

The opinion of Escherich and Quest is in accordance with the recent investigations of Voetglin and McCallum,¹¹ who revealed the fact that the calcium excretion of parathyroidectomized animals was increased and the tetany attacks could be eliminated by calcium salts injection.

Therefore, we conclude that infantile tetany is due to insufficiency of the parathyroid glands produced by hemorrhages.

Before discussion of the adult tetany we wish to report our case, that of a man, aged twenty-six years, a Russian, speaking little English, a butcher by occupation. He was admitted to the Allegheny General Hospital, May 25, 1909, in the service of

⁸ Virchow's Arch., ccciii, Heft 2.

¹⁰ Jahrb. f. Kinderheilk., 1905.

⁹ Die Tetanie der Kinder.

¹¹ Jour. Exper. Med., 1909, xi, No. 1.

Dr. McNaugher, to whom we are under obligation for permission to examine the patient and to make this report. One week after admission, and two weeks after the onset of the disease, the patient died.

He had never been sick before the present illness except with an attack of influenza. His employer reports that he drank large quantities of pure alcohol and smoked cigarettes excessively. There was no history or sign of an infected wound.

Two weeks before admission the patient fell off a porch, a distance of five feet, and sustained an injury to the spine in the region of the third or fourth lumbar vertebræ. One week after this accident (two weeks before his death) he developed the first symptom of his fatal illness, an attack of rigidity in the arms and legs. These attacks came with increasing frequency and severity. When he was admitted to the hospital the attacks of rigidity affected the arms, legs, and trunk, including the neck. These attacks were intermittent and accompanied by considerable pain in the arms and legs, especially the latter. On admission, he complained much of pain in his legs. He asked to have his knees flexed, as he said this afforded great relief. It was noted that the patient became quite cyanotic during spasms, and that he perspired profusely.

May. 25. Sputum was negative for tubercle bacilli. The urine showed a slight trace of albumin and some hyaline casts.

May 28. Lumbar puncture was made, but resulted in a dry tap. The Wassermann test was negative.

Blood: Hemoglobin, 75 per cent.; red blood cells, 4,100,000; leukocytes, 7600. Differential count: Polynuclear neutrophiles, 78 per cent.; large lymphocytes, 11 per cent.; small lymphocytes, 10 per cent.; monocytes, 1 per cent.

On May 28 the patient was examined by Dr. Diller. The patient's mental condition seemed clear. Handling the arms and legs produced generalized spasms, which kept up for a minute or two. Pressure on the legs, even light pressure, caused a generalized spasm affecting the arms, legs, and trunk, and neck muscles. His position became one of opisthotonos; arms and legs were hyperextended. The legs were more involved than the arms. There were no spasms of the fingers and toes, and none of the face muscles; but pressure over the seventh nerve produced facial spasm. The masseters (especially examined) were free from spasms. Knee-jerks were slightly increased; there were no Babinski signs.

The same day the eye-grounds were examined by Dr. A. C. Blair and found to be normal. The nurse noted that the spasms came particularly when the patient attempted to raise his knees; and in his examination, Dr. Diller noted the same. The spasms now came spontaneously without handling of the limbs, but they were especially provoked by handling or pressure anywhere on the legs or arms, especially the former.

On June 1 the patient was again examined by Dr. Diller. Prior to this his temperature had been normal, but his pulse had been accelerated, ranging from 90 to 120. On this day his temperature suddenly shot up to 103° , and he died a few hours later. For the preceding three days he had had no spasms in the daytime, but they were especially severe at night. At this examination no spasms were produced by pressure of the arms and legs, even when made over the vessels and nerves, but there was resistance in both arms and legs to passive movements. There were no spasms of the masseters, but considerable stiffness of the neck muscles.

The patient died a few hours after this examination was made.

The autopsy showed an external fibrous pachymeningitis, chronic leptomenigitis, edema, and hyperemia of the brain, hyperemia of the spinal cord, bilateral adhesive pleuritis, spleen slightly enlarged, hemorrhagic gastro-enteritis, hyperemia of kidney and liver, with slight parenchymatous cloudiness.

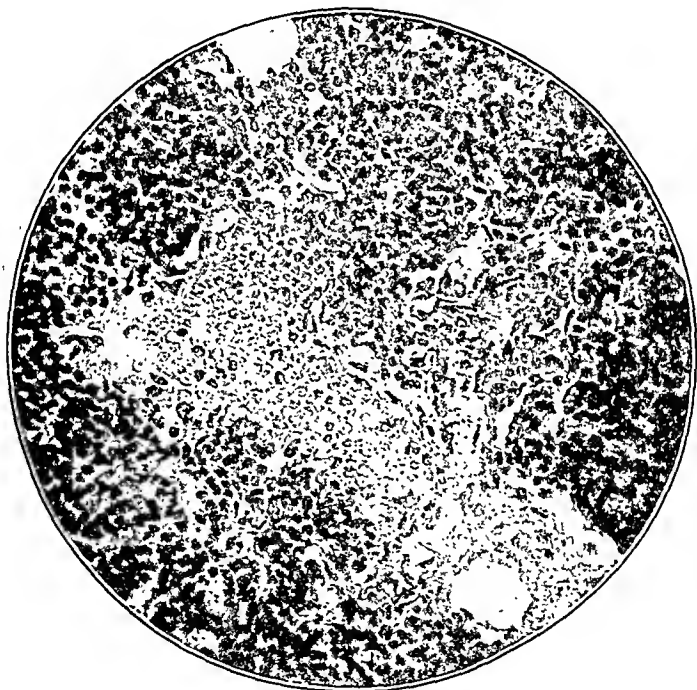


FIG. 1.—Ruptured bloodvessel with perivascular hemorrhage. Lcitz, objective 5; ocular 4.

Special attention was given to the examination of the parathyroid glands, which in this case were found without any difficulty. Two were on the right side and one on the left side. The two former measured 10 mm. long by 3 mm. broad, and 9 mm. long by 2.5 mm. broad, while that on the left side measured 11 mm. by 3 mm. broad. Macroscopically the glands were opaque and brownish in color, with red punctations having the appearance of hemorrhages. The symptoms of tetany could not be accounted for by

the macroscopic changes found at autopsy, except for the suspicion of hemorrhages of the parathyroid glands. The pachymeningitis, leptomeningitis, and gastro-enteritis were probably of alcoholic origin.

Microscopic Examination of the Organs. The changes in the three parathyroid glands were almost uniform. With low power, extensive infiltration of the parenchyma with large fat cells was noted, causing partial atrophy. The connective-tissue stroma was greatly thickened and divided the parenchyma into various sized lobules. Bloodvessels and capillaries were greatly distended. With higher power the parenchyma consisted largely of small, indistinctly outlined epithelial cells which were rich in chromatin

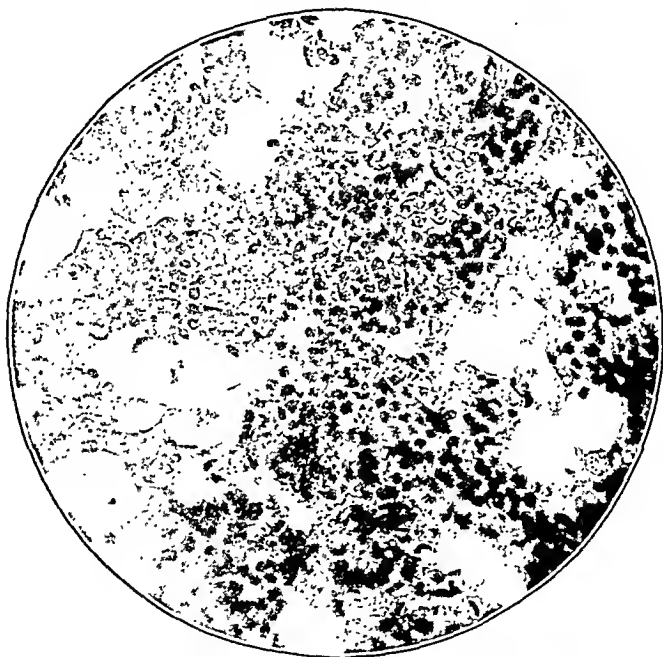


FIG. 2.—Parenchyma invaded by profuse hemorrhages. Leitz, objective 5; ocular 4.

(cell type II). The protoplasm stained bluish red. On the edge of the gland were found large, compact, distinctly outlined polygonal epithelial or oxyphile cells (cell type I). The protoplasm of these cells was finely granular, somewhat cloudy, and stained fairly well with cosin. The small intercellular mass stained more deeply with cosin. The nuclei of the cells were not so rich in chromatin as in cell type II, and as in some near the periphery. Some cells were without nuclei. Small groups of the same cells were found inside of cell type II.

The fine granulated appearance and the bluish-red color of cell type I and II suggested a slight parenchymatous degeneration. In

normal epithelial cells the protoplasm stains deep red with eosin, or is nearly colorless.

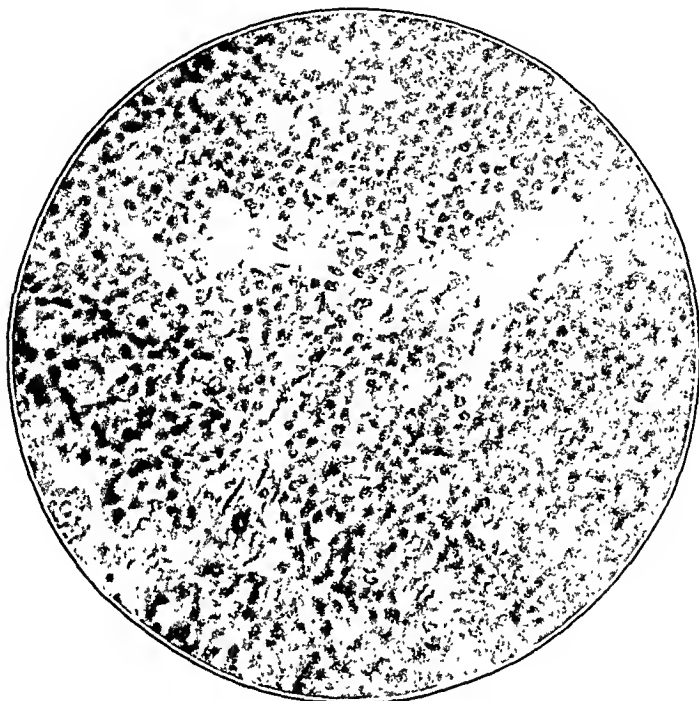


FIG. 3.—Same as Fig. 2. Leitz, objective 5; ocular 4.

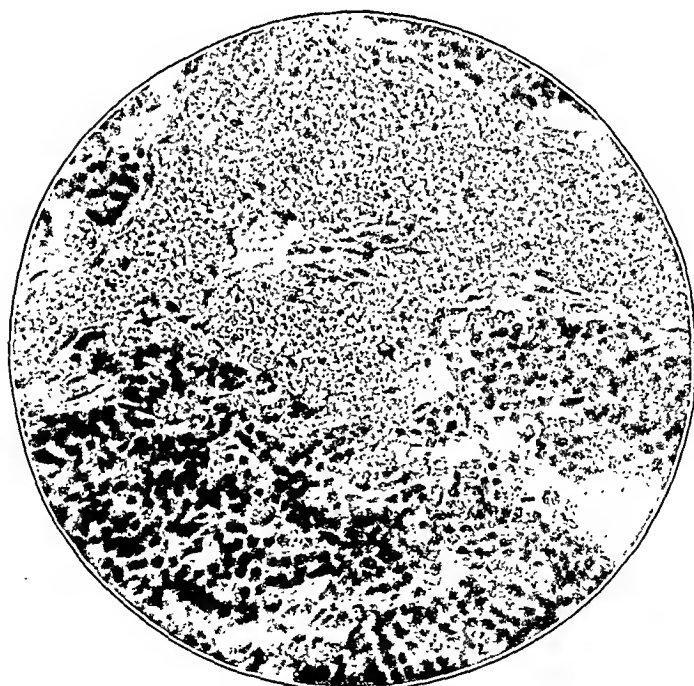


FIG. 4.—Same as Fig. 1. Leitz, objective 5; ocular 4.

The most interesting morbid change in the glands was the multiple hemorrhages which were diffused throughout one-half to two-thirds of the parenchyma in the form of small circumscribed areas. These hemorrhages could be traced to medium-sized blood-vessels. Larger perivascular hemorrhages, as found in the parathyroid glands of children, were not noted. The appearance of the hemorrhages was as follows: The red blood cells lay directly on the epithelial cells, which could be demonstrated with the Van Gieson stain. In contrast with the distended bloodvessels and capillaries fine, spindle-shaped endothelial cells were seen, deeply stained and at regular distances apart, which differentiated them from a hemorrhage. The fibrous adventitia of the vessels showed slight hyaline degeneration. Some vessels had very small lumina. The walls of the veins were much distended. In some places drops of colloid inside of glandular-like formations of epithelial cells were seen.

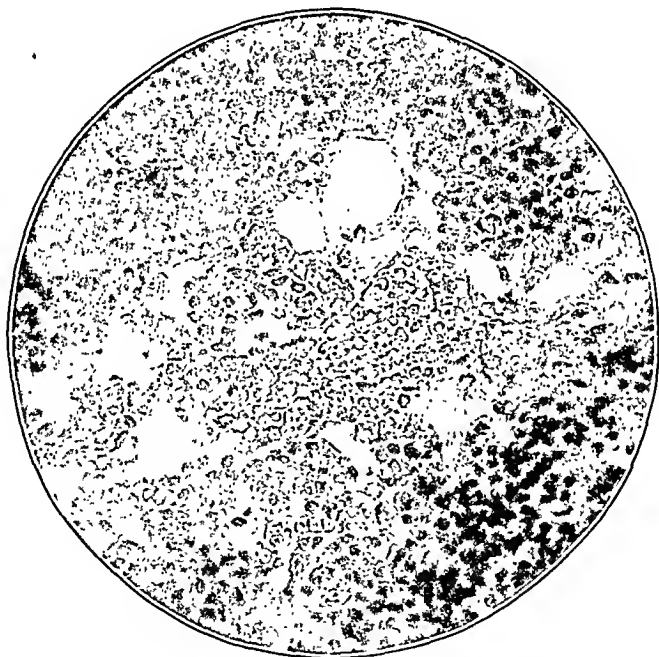


FIG. 5.—Same as Figs. 1 and 4. Leitz, objective 6; ocular 4.

Retrogressive changes of the hemorrhages, such as pigment, were not found, and this led to the conclusion that the hemorrhages must have been of recent origin.

The red blood cells presented a peculiar appearance. Some of them appeared deeply stained with eosin and were distinctly outlined. Others were merely visible and were stained very lightly. One received the impression that the hemoglobin had been extracted from them. We believe that this phenomenon is not due

to incomplete fixation. Petersen¹² has called our attention to this phenomenon. In his opinion the deeply stained bloodvessels are loaded with colloid, which is transported by the red cells through the organism. But we are not prepared to accept this view.

Microscopic Examination of the Central Nervous System. Numerous sections of the cortex and spinal cord, stained after Nissl, showed that the large pyramidal cells in the cortex were degenerated (absence of tigroid and vacuolation); some cells were without nuclei. The dendrites were greatly elongated. Practically the same change was found in the large cells of the anterior horns of the cord. No noteworthy change was seen in the white matter or the bloodvessels. The cells in the spinal ganglia were without change, and the peripheral nerves appeared normal.

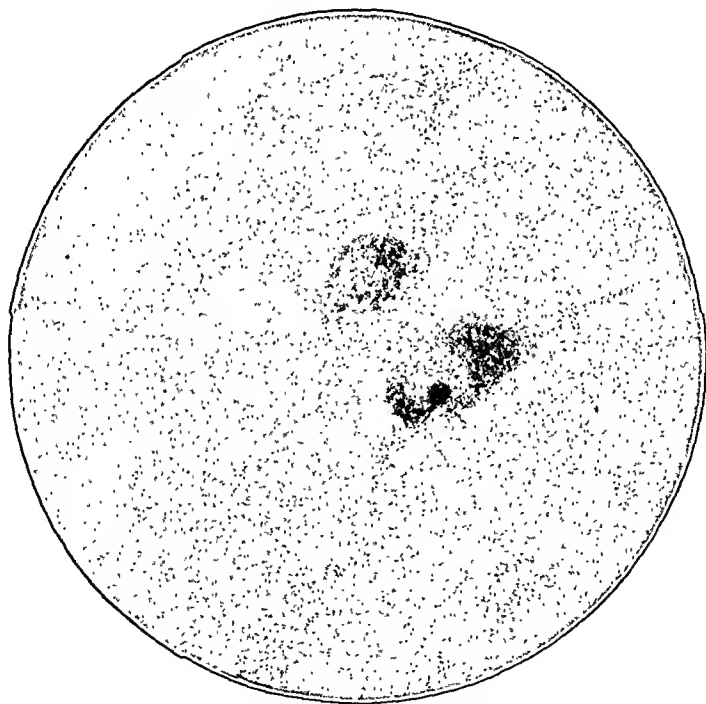


FIG. 6.—Large pyramidal cells of cortex of the frontal lobe of brain, stained after Nissl, showing prolongation of dendrite and absence of tigroid. Leitz, $\frac{1}{12}$ oil immersion; ocular 4.

The kidney and liver showed slight parenchymatous cloudiness, and their bloodvessels were greatly distended. The mucous membrane of intestine and stomach showed a few small hemorrhages.

In addition to our case, we review briefly the cases of tetany adutorum which can be divided into three groups.

Group I. Four cases of Haberfeld,¹³ with typical clinical symptoms of tetany and changes of the parathyroid glands, found at autopsy. Case I showed amyloid degeneration of the small blood-

¹² Loc. cit.

¹³ Loc. cit.

vessels and cyst formation of the large polygonal cells. Cases II and III showed hypoplasia, with cicatrix due to previous disease. Case IV, the first case of tetany gravidarum studied, showed hypoplasia and cicatrix of the parathyroid glands. This group may be named "hypothyroidismus."

Group II. One case of McCallum,¹⁴ with typical clinical tetany, and no parathyroid glands found at autopsy (apathyroidismus).

Group III. Three cases of Erdheim,¹⁵ two of gastric tetany and one from brain tumor; one case of Koenigstein, carcinoma of the pancreas, all with typical clinical tetany, and no microscopic changes in the parathyroid glands.

The question arises as to whether any relation exists between tetany adutorum and the parathyroid glands. Cases under Group I and II are undoubtedly due to disease of the parathyroid glands. As above stated, the recent investigations of Haberfeld have proved atrophy of the parathyroid glands to be the chief cause of infantile tetany, and in all probability it is also the cause of tetany adutorum.

McCallum's case of apathyroidismus stands isolated, and its explanation is difficult. The apathyroidismus was either due to a congenital defect or a destructive lesion of the glands.

In our opinion it is not likely that it was due to a congenital defect, because the individual would not have lived so long without symptoms of tetany, but on account of their probable atrophic condition the parathyroids might have been overlooked. On the other hand, there might have been a lesion attended with complete destruction of the glands, thus causing tetany, or possibly there might have been an acquired serogen or histogen immunity to tetany toxin which has been demonstrated by animal experiments (Blum). Finally, the individual may have died from acute intoxication from tetany toxin, which could not be neutralized.

How may we account for the third group where no microscopic change of the parathyroid glands was found?

We believe that in such cases there was a hypoparathyroidismus due to atrophy of the gland without any other microscopic change.

The study of these cases was during the earliest investigations of the epithelial body, when the significance of the atrophy of the gland was not taken into consideration.

Our knowledge of the pathological anatomical changes in the parathyroid glands is limited. The latest investigations show that the parathyroid glands are very rarely diseased, at least we find in the literature very few observations of typical pathological changes.

Infiltration of the glands was found in leukemia, pernicious anemia, bacterial emboli with metastatic abscesses by Erdheim

¹⁴ Die Beziehung der parathyreoiddrüsen zur Tetanie, Ztbl. f. allg. Path. u. path. Anat., lxxvi, 1905.

¹⁵ Loc. cit.

and Yanase; tubercular and syphilitic inflammation by Pepere,¹⁶ Benjamin, Schmorl,¹⁷ Koenigstein,¹⁸ Carnot and Derion,¹⁹ Verebely,²⁰ Stumme, Yanase; tumors, myoma, by Pepere; adenoma by De Lauti, Erdheim, Benjamin, and McCallum; lymphoma and angioma by Askanazy, Weichselbaum, and Verebely.

In all these cases these findings were accidental as no tetany was observed.

Hemorrhages in the parathyroid glands of adults without tetany were found by Erdheim in a man, aged forty-five years, who died of tuberculosis.

Pepere found hemorrhages in 2 cases: one, a girl, aged eighteen years, with a heart lesion and hemorrhages and cyst formation without pigment in one parathyroid gland; the other, a man, aged eighty-two years, without special clinical and anatomical findings, with fresh hemorrhages in one gland.

Verebely found rather recent hemorrhages in two glands, hematoxylin pigment in surrounding tissue, in a man, aged thirty-eight years, the cause of death is not mentioned.

Our case is the first in which an adult with tetany and hemorrhages of all parathyroid glands was observed. We believe the hemorrhages were all of recent occurrence, because no pigment was present. All three glands showed more or less primary atrophy of the parenchyma, followed by hemorrhages, which we believe were the indirect cause of the tetany.

Here the already atrophic glands were rendered insufficient by the hemorrhages.

In the infantile tetany we have first the hemorrhages which produce the atrophy of the glands.

According to Haberfeld²¹ the diseased epithelial bodies are not alone responsible for the tetany, and a person could live for a long time with changed glands until disturbances, such as intestinal auto-intoxication, pregnancy, etc., would cause increased activity, which leads to tetany. Therefore, the insufficiency of the parathyroid glands is the chief cause of tetany.

He distinguishes between absolute and relative tetany. The absolute is derived from the absence of the epithelial body (operative tetany). The relative tetany is caused by increased metabolic products, which cannot be neutralized by the normal parathyroid glands or by a normal amount of metabolic products which cannot be neutralized by the insufficient parathyroid glands.

His latest investigations prove that changed parathyroid glands

¹⁶ Leghiandole paratiroidica. Turin 1906; Arch. d. Anat. e di Embriol., viii, fasc. 2, 1909; Arch. de méd. expér., January, 1908.

¹⁷ Münch. med. Woch., 1907.

¹⁸ Ges. f. inn. Med. u. Kinderheilk., December 6, 1906.

¹⁹ Compt. rend. dela Soc. de Biol., 1905.

²⁰ Virchow's Arch., 1907, clxxxvii.

²¹ Die Epithelkörperchen bei Tetanie und bei einigen anderen Erkrankungen, Virchow's Arch., cciii, Heft 2.

plus increased metabolic activity is the chief factor in producing tetany, and "in infantile tetany this seems to be a law."

The disturbances are also the predisposing cause, the exciting cause being of unknown source.

Some investigators, especially Koenigstein, claim that the microscopic change in the gland is not sufficient to account for the clinical symptoms of tetany, but this opinion cannot be accepted.

All variations of the pathological process in the parathyroid gland lead to disturbance or decrease in their function.

A few referred diseases²² of the parathyroid glands are not recognized by Erdheim and Habersfeld.

The hyperplasia of the gland found by Erdheim in osteomalacia remains to be studied. At present we can only say the diseased parathyroid glands cause tetany; as to other diseases, nothing has been demonstrated.

The real etiology of tetany is unknown, but it seems to be of an enterogenous origin. Without doubt the glands have the functions to avert and deintoxicate certain toxic products (autoneurotoxins), which are formed during metabolism, and which have a great affinity for the central nervous system. They also play the role of a protective apparatus for the central nervous system.

The clinical observation and pathological examination in conjunction with animal experiments have solved one of the most difficult problems of the ductless glands, and it is hoped that the real etiology of the tetania parathyreopriva will soon be made clear.

RHEUMATIC MYOSITIS.

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THE particular phase of the large subject of muscular rheumatism considered in this paper is the relation of certain acute inflammatory conditions of the muscles to acute rheumatic fever. Chronic muscular rheumatism was fully described so long ago as 1816 by Balfour. Rheumatic involvement of muscles was also extensively studied by the Swedes, notably by Froriep, in 1843, and Helleday, in 1876. They, however, paid more attention to the chronic nodular condition and its treatment by massage. Considerable was written about the subject of acute myositis in the

²² Eclampsia gravidarum (Vassale Zanfrognini), paralysis agitans (Lundborg), myasthenia gravis pseudoparalytica (Lundborg and Chvostek).

German literature in a period of about five years from 1892 to 1897. A number of series of acute cases, some epidemic in character were reported and the general consensus of opinion at that time was that they were infectious and identical with acute articular rheumatism or the same in an attenuated form. Some even claimed that many of the mild cases reported as dermatomyositis were of the same nature. There is little doubt that the condition has been variously diagnosticated, as the cases to be reported later well illustrate. The English literature on the subject is scanty. In the last year several articles have appeared, but like the Swedish writings, mostly with reference to the chronic muscular conditions under the name of fibrositis or nodular fibromyositis, which is described as independent of acute rheumatism or, indeed, any acute myositis. The French literature is also scanty. However, Rose,¹ under the heading of muscular cephalalgia, although describing the chronic fibrositic condition, refers to rare acute cases, which subside under salicylates and mentions acute muscular and articular rheumatism in the etiology.

In that period of interest (1892-1897) in the German literature, when these cases of acute myositis were more recognized than at any time since, the subsequent condition of a nodular infiltration (*Rheumatische Muskelschwiele*) was repeatedly described, sometimes in cases that had definite joint and muscle involvement at the same or different times, sometimes when only the muscle was involved. The infection of rheumatic fever may not be the only cause of the recently exploited fibrositis, especially if, as was done by Luff, one includes under that heading such obviously different fibroid processes as Dupuytren's contracture.² But, the first question is whether a specific rheumatic myositis exists, that is, as a local manifestation of the generalized infection of rheumatic fever, the same as arthritis, phlebitis, or iritis. Various writers have inferred that the condition was an established fact (Kerr³), yet in the rather detailed classification of the inflammatory conditions of the muscles in Albutt and Rolleston's series, there is no mention of it. One case is described in Osler's series.

Before considering further the etiology of this condition the following cases from the Medical Dispensary of Lakeside Hospital may be reported:

CASE I.—This case is so typical that it may be reported at some length. Miss L. M. came to Lakeside Dispensary for the first time in 1897 complaining of blurred vision. A diagnosis of interstitial keratitis was made, and a few ridges on the teeth were regarded as confirmatory evidence of congenital syphilis. The clouding all cleared up after about four or five months of antisyphilitic

¹ Sem. Médicale, vol. xxxi, pp. 145, 156.

² Amer. Jour. Obst., vol. lxiii, p. 931.

³ Lancet, 1910, i, 712.

treatment. One year later the same condition recurred in the other eye. This also cleared up with the same treatment. In the summer of 1900, the patient returned to the Medical Dispensary with a painful swelling of her left arm in the upper outer part. She had never had acute rheumatism or any infectious diseases that would have any bearing on the case, except the specific keratitis. Evidently the swelling was suspected to be an abscess, as it was incised in the dispensary. There was no suppuration and the wound healed rapidly, leaving the swelling the same. She was then given a course of antisyphilitic treatment without improvement. In August of 1900 she was sent into the hospital on the surgical service. A general anesthetic was given, and a second larger incision was made. The record of the operation reads as follows: "Over the periosteum was a layer of velvety gelatinous material. An attempt to curette this away failed, so all the tissue was chiselled away, down to firm bone. The wound was packed wide open. Subsequently it was noted that there was only rather free serous discharge from the wound, and that healing took place rapidly. The swelling was still distinct, although somewhat less at the time of her discharge, August 14, 1900.

After this experience she did not return to the hospital until the fall of 1911, when she appeared at the Medical Dispensary and related the following history: She went to a physician outside who treated her arm mostly by counter-irritation over a period of six months. The condition in her arm then practically disappeared, but left some indefinite soreness, for which she had several treatments by a masseur. All symptoms then disappeared and never again recurred in the same location. Several years later she had another swelling over the upper end of the sternum which was also incised to drain a supposed abscess, but no pus was obtained. In 1901, that is, previous to the second obscure swelling, she had a typical attack of acute articular rheumatism, and in 1904 a second, and in March, 1911, a third. With the last attack the right temporal muscle and the lower third of the quadriceps extensor femoris became swollen and painful. The patient thinks these swellings were of the same nature as those of the arm and sternum. The thigh swelling subsided promptly. The right temple, however, remained swollen, indurated, and painful, and caused constant headache. After enduring this for about two weeks, she appeared at the Medical Dispensary with the temporal muscle rounding out from the zygoma to the temporal ridge prominently enough to give a rather ludicrous contour to her otherwise small narrow face. At this time there was also marked chronic endocarditis with mitral insufficiency. She was given 15 grains of sodium salicylate four times a day, but returned in a few days unimproved. She was then given 15 grains every two hours with an alkali until toxic. The pain disappeared in one day. The swelling was nearly all gone in three

or four days, leaving some diffuse induration. Since then the swelling has recurred at intervals of three or four weeks, each time being relieved by salicylates. During October, 1911, the condition became more continuous and chronic, and reacted less favorably to salicylates. Since then she has been treated by massage, and is regarded as a case of indurative headache, as described by Edinger.⁴

A few other cases may be reported more briefly.

CASE II.—Boy, aged fifteen years. Mother rheumatic. Patient had measles, mumps, pertussis, and diphtheria, but no tonsillitis or acute rheumatism until the present illness, which began with sudden pain in the wrist, shoulder, and ankle. After about two days the upper half of the right arm swelled up over night, and remained so for a week or more, during which time the joint symptoms had subsided. He was then admitted to the hospital with a temperature of 101°, the right arm the seat of marked swelling of a firm elastic character, skin redness, and so much pain and loss of power that the arm lay helpless at his side. Acute osteomyelitis was considered in the diagnosis. Two x-ray plates were negative. The blood examination was as follows: Leukocytes, 8,800; hemoglobin, 95 per cent.; Differential count: Small mononuclears, 21 per cent.; large mononuclears, 5 per cent.; polymorphonuclears, 69 per cent.; eosinophiles, 4 per cent.; transitionals, 1 per cent. He also had at this time a slight mitral insufficiency. He was rendered toxic with salicylates with prompt relief. The swelling subsided gradually. At the end of three weeks his arm was painless, but the biceps and the upper part of the brachialis anticus were rather thickened and indurated.

CASE III.—Mrs. M. C., aged thirty-nine years. Two weeks after the onset of acute articular rheumatism involving both knees and ankles there appeared swelling and tenderness of the upper part of both thighs, more marked on the right, also tenderness in the lower two inches of the biceps muscle and its tendon on both sides. Three days later, after being rendered toxic with salicylates, both thighs were one inch less in circumference, measured at the same level, and there was much less pain.

There have been 2 other cases less acute, but with distinct muscular swelling involving the left scapular muscles and right trapezius respectively. Also another case of indurative headache without swelling when observed, but with tenderness along the attachment of the temporal muscle.

In this connection a case may be reported from the private practice of Dr. John Phillips, with his permission. The patient was a well developed women, aged thirty years. Her general health was good and there was no alcoholic history. One year ago she had a rather mild attack of acute rheumatism with pain and

⁴ Modern Clinical Medicine, Diseases of the Nervous System, p. 863.

swelling of both shoulders and a temperature of 101, associated with brachial neuritis and tenderness above the clavicle on the right side and tenderness over all the nerves of the arm. There was almost complete loss of power. She was put on oil of winter-green until toxic. The acute pain subsided in two or three days, and the neuritis in two weeks, although it was five weeks before the strength in the arm was regained. At the same time she had severe headache and tenderness of the scalp, with thickening of the insertions of the sterno-mastoid and trapezius muscles of sufficient degree as to be discovered by the patient. This thickening disappeared under massage and salicylates in about 48 hours. Five months ago she had a similar condition of the muscles of the head with some weakness of the left arm and tenderness over the ulnar and median nerves. The headache again yielded to salicylates and massage. The neuritis cleared up in about three weeks. There was no endocarditis.

In the first 3 cases it seems highly probable that the myositis was only a part of the generalized infection of acute rheumatic fever. Of course, there is no bacteriological evidence of this fact, which would be difficult to prove, since the specificity of the micrococcus rheumaticus or any other organism is not established.

In this connection several convincing series of cases may be brought together from the literature. In 1894, Newton,⁵ of Kent, reported an epidemic of 43 cases of acute muscular rheumatism seen within five weeks. The abdominal and lower intercostal muscles were most commonly involved, rendering respiration painful, short, and rapid. In some cases various muscles of the back, especially in the lumbar and sacral regions, were effected. The onset was acute, with fever of 100° to 104°; pulse, 80 to 100; furred tongue, headache, and the characteristic sour acid sweats of acute articular rheumatism. There were no nasal or pulmonary complications, which is of importance in making the differential diagnosis from influenza. Newton regarded the infection as identical with acute articular rheumatism for reasons, which he summarizes as follows: (1) There was no influenza prevalent at the time. (2) There was none of the subsequent depression characteristic of influenza. (3) They responded promptly to salicylates. (4) It was apparently mildly contagious, 3 cases occurring in one household. (5) There was endocarditis in 2 of the 43 cases; these were not treated with salicylates. (6) The epidemic occurred after an unusually wet summer and low in the valley of the Medway.

As stated before most of the reports of acute muscular rheumatism appeared in the German literature during the period of 1892 to 1897. Among the writers who expressed the opinion that the condition was the same infection as acute articular rheumatism,

⁵ Brit. Med. Jour., vol. xi, p. 651.

were Sahli,⁶ Rosenbach, von Leube,⁷ Immermann and Saccharjin.⁸ Risse⁹ thought, as referred to above, that some of the cases reported as dermatomyositis were really the same thing. He reports a case in a man, aged thirty-five years, who had had acute articular rheumatism with two recurrences. His parents were also both rheumatic. The illness reported began with acute rheumatism of both ankles. After one week, the right thigh and the right tibialis anticus and peroneal muscles became tender, swollen, and indurated. Salicylates relieved the acute pain but in two days the calf and the other thigh muscles and overlying skin became tense and edematous. The testicles and abdominal wall then became similarly involved, and some hiccough occurred, suggesting slight disturbance of the diaphragm. The case was also complicated with nephritis, lasting about four weeks. Risse thought the dermatitis and edema might simply be due to a more intense or virulent rheumatic infection. He also thought that the chronic condition (*Muskelschwiele*) when not traumatic, was usually referable to acute rheumatism.

Sick¹⁰ reported an instructive series of 9 cases occurring in epidemic form among nurses and attendants living in the basement of a hospital. These patients were well studied clinically and by blood and tissue examinations. Symptoms were initiated in some cases with sore throat, in all cases with malaise, gastric disturbances and general indisposition, followed in one to three days by rise of temperature and pain, swelling, and a diffuse or nodular infiltration of various muscles, usually of the thighs, calves, back, or arms. The skin was not affected and the lungs were clear. There were no neurological changes. There was excessive perspiration, and one case was associated with typical articular rheumatism. This case had had one year previous to the illness in question, acute pain in the right iliac region, with fever, and was operated on for appendicitis (during the febrile stage), but the appendix was found normal. Later she had joint swellings, then this epidemic muscular involvement, at which time a mitral insufficiency was observed; and finally, following this, an attack involving joints and muscles simultaneously, both of which were relieved by salicylates. All of these cases were characterized by a strong tendency to recurrence. Blood cultures were uniformly negative. There was no leukocytosis or eosinophilia. Excised portions of muscle showed no histological change, except in one case, in which there was some clouding of the structure and slight infiltration with fine fat droplets and round cells. No trichini were found. Bacterial stains of the tissues were also negative.

⁶ Deutsch. Archiv. f. klin., Med., 1893, Band li.

⁷ Deutsch. med. Woch., 1894, Band i.

⁸ Ibid., 1897, p. 232.

¹⁰ Münch. med. Woch., 1905, lii, 1092 and 1152.

⁸ Ibid., 1894, p. 525.

Sick considered in the diagnosis here, trichinosis, dermatomyositis, Gregarinal myositis (better known to veterinary medicine), and acute rheumatic fever. The tissue examinations excluded all but dermatomyositis and rheumatic fever. Sick did not class it as a rheumatic myositis, because it did not conform to the description of that condition given by Lorenz,¹¹ who gives four characteristics, namely: (1) Short duration, (2) limited localization, (3) no histological changes, and (4) no infiltration of muscle. His description, however, evidently does not apply to the acute form of myositis. Although Sick classified the condition as an attenuated form of dermatomyositis, he admits the disturbing factor of an associated typical articular rheumatism in one case. The involvement of the respiratory muscles he regarded as inconsistent with muscular rheumatism, but this was a prominent feature of the cases reported by Newton, above summarized. As to dermatomyositis, the perivascular inflammation of that disease was lacking in Sick's cases.

Herz¹² also believes there were many mild cases of dermatomyositis reported at that time, which he considered identical with acute rheumatic fever. He reported 21 cases from Breslau, with 9 recoveries. Some of these cases had joint swellings, also involvement of the tendons and tendon sheaths as well as of the muscles. The skin involvement was in the form of an erythema which resembled erysipelas, and which subsided early, leaving the myositis as the prominent feature of the disease. The skin sensibility was intact, and the electrical reactions showed at most occasional diminished excitability. One of the severe cases, fatal in six days, was autopsied, and the findings reported as follows: Bronchitis and edema of lungs; a few small infarcts of the spleen, marked softening and edema of the muscles with beginning suppuration. A culture taken twelve hours post mortem showed an organism of the colon group, which Herz regarded as a secondary infection.

V. Leube¹³ reported on 200 cases of muscular rheumatism from the Wurzburg Clinic. He describes its greater prevalence, in almost epidemic form, in the spring, and expresses very strongly the opinion that it is identical with acute articular rheumatism and that only the bacteriological evidence is lacking. He also speaks of the frequent muscular involvement in ordinary acute articular rheumatism, a fact which is scarcely referred to in recent textbooks. His cases usually had considerable constitutional disturbance; many, however (two-thirds of all), especially the mild ones, had no fever. He reports one-sixth of all cases as having endocarditis.

Lacquer¹⁴ reported a case of special interest in connection with Case I reported above, from Lakeside Dispensary. It was an

¹¹ Jour. Exp. Med., 1898, No. 30.

¹² Loc. cit.

¹³ Deutsche. med. Woch., 1894, p. 791.

¹⁴ Deutsch. med. Woch., 1896, p. 442.

acute and recurrent myositis of the upper arm, which was incised on two occasions, three years apart, but there was no gross or histological change in the muscle or periosteum. This case later had typical acute articular rheumatism. Lacquer regarded the myositis as of the same origin, probably in attenuated form.

Kerr¹⁵ says there is no doubt of the fact that acute rheumatic fever may have as its first manifestation, involvement of the abdominal musculature, and reports 3 cases all in children at some time subjects of acute articular rheumatism. For example, 1 case had a sudden onset of localized pain and swelling in the abdominal musculature, with temperature of 100.4°, which subsided under salicylates. Three months later the child had a typical attack of acute articular rheumatism. He is personally convinced that the two differently localized affections are parts of the same disease.

In conclusion, then, if one may accept genuine rheumatic myositis as a definite clinical entity, the question arises as to its relation to the recently described fibromyositis, indurative headache, etc. Undoubtedly the chronic nodular rheumatism (*Muskelschwiele*) of the German literature would fall under this heading. However, the recent articles of Telling,¹⁶ and Luff,¹⁷ etc., give it a wider application, and include various fibroid processes of the skeletal musculature. Telling does not think that it is a sequel to acute rheumatic fever, or that it occurs with any frequency in genuinely rheumatic cases. However, Stockman,¹⁸ from whose article Telling and others quote as the most complete in the scanty literature on the subject, thought that acute rheumatism was one definite cause of the chronic form, and that the subcutaneous nodules of acute rheumatism frequently persisted as indurations or thickenings of fasciæ, nerve sheaths, etc. These thickenings he considered responsible for the neuralgic pains and even atrophy following acute rheumatism. He also suggested that the nodules may be definite localizations of the infecting organism, but that the treatment required to relieve the condition at this stage was different from that of active rheumatic fever. Miller¹⁹ also described the subacute form of myositis with slight swelling of the muscle and pain on pressure and voluntary movement, and slight effusion into the subcutaneous tissues over the muscle after the myositis has subsided. Hence it seems probable that some cases of fibrositis may follow a previous acute rheumatic myositis, which may have been mild or unrecognized. All writers, English, German, Swedish, and French agree that massage is the only really efficient treatment. This should be carried out systematically and with the idea of dispersing the infiltrations.

¹⁵ Loc. cit.

¹⁶ Lancet, 1911, i, 734.

¹⁷ Loc. cit.

¹⁸ Edinburgh Med. Jour., vol. xv, p. 107.

¹⁹ Trans. Med. Chir. Soc., Edinburgh, 1897-8, xvii, 188.

ADAMS-STOKES SYNDROME, WITH COMPLETE HEART-BLOCK AND PRACTICALLY NORMAL BUNDLE OF HIS.

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THE case herewith described was first reported by Dr. Alfred Stengel and Dr. William Pepper in the *AMER. JOUR. MED. SCI.*, October, 1910, under the title, "Heart-block, with an Indication of Genuine Hemisystole." From that time onward the patient was almost constantly under observation, and many more pulse tracings were obtained before his death. An autopsy was held and a careful examination of the heart was made. The full pathological report follows later, but suffice it here to say that the bundle of His was practically normal. In addition to this interesting finding, several other features make us believe this further report on the case is fully justifiable.

Six cases have been previously reported of heart-block without any lesion of the bundle of His, or with but such slight alteration of the bundle, as might be expected in many hearts where no block had occurred.

Krumbhaar,¹ in 1910, in his article on "Adams-Stokes Syndrome, with Complete Heart-block, without Destruction of the Bundle of His," states that he could find but 2 cases similar to his own, and since that time we have been able to find but 3 additional cases.

DENEKE AND FAHR'S² CASE. This case was one of complete block. The authors admit that they did not succeed in completely examining the bundle which was abnormally long but found no lesion in the parts examined.

NAGAYO'S³ CASE. Here the heart-block was only incomplete. No lesion of the bundle was found, but there was extensive myocarditis, and Nagayo believes that the block occurred through the altered musculature of the ventricle.

¹ *Arch. of Int. Med.*, 1910, v, 583.

² *Arch. f. klin. Med.*, 1906, lxxxix, 39. See also *Virchow's Arch.*, 1907, clxxxviii 562.

³ *Zeit. f. klin. Med.*, 1909, lxxvii, 495.

KRUMBHAAR'S⁴ CASE. Here complete heart-block with Adams-Stokes syndrome was known to have existed for five years. At autopsy a chronic myocarditis of the ventricles was found. The bundle of His was traced in unbroken continuity from Tawara's node to beyond the bifurcation, with no abnormality other than a slight increase in connective tissue, no greater than is found in other hearts that have never exhibited heart-block. Fibrous changes were found in the muscle bundle of Keith in the sino-auricular junction.

GRIFFITH AND COHN'S⁵ CASE. This is a case with lengthened *a-c* interval and with attacks of partial and complete heart-block, and showed the bundle of His continuous from the auriculo-ventricular node to the bifurcation, although its diameter was somewhat reduced and the fibers compressed by diffuse fibrosis. Beyond the bifurcation it was interrupted by granulation tissue.

MALLARD, DUMAS, and REBATTU'S⁶ CASE. This was a case of partial block when tracings were made, but in which probably complete block had occurred at times, as spells of unconsciousness are mentioned. At autopsy there was an extensive fibrous mediastinitis, with involvement of the vagi. The region of the bundle of His was sectioned and but one in twenty of the sections stained. No lesion was demonstrated.

HOLST AND MONRAD-KROHN.⁷ The authors report a case of a male, aged fifty-four years, who for eight days had repeated attacks of syncope, with disappearance of the radial pulse. Between the attacks the pulse varied from 40 to 80. Tracings showed at times a partial block. At other times a slowing of both auricle and ventricle. At autopsy no lesion of the *a.-v.* bundle was found, except that it was slightly more fatty than usual. Both vagi, however, showed evidence of extensive degenerative neuritis. The authors believe the cardiac attacks to be of vagal origin.

AUTHOR'S CASE.

The following chronological list of events will serve graphically to place the patient's life on view:

1871, born in Italy. 1894, syphilis, in Philadelphia Hospital. 1900, married. 1902, wife aborted. 1903, child born, died from burns. 1905, child born, living and well. 1906, child born, living and well. 1907, child born, living and well. 1907, patient had attacks of epigastric pain. 1908, child born, living and well. Patient fainted. 1909, severe pains and syncopal attacks. January 25, 1910, pains. February 5, admitted to University Hospital,

⁴ Loc. cit.

⁵ Quart. Jour. Med., 1909-10, iii, 126.

⁶ Arch. des Maladies du cœur, Paris, 1911, iv, 298.

⁷ Quart. Jour. Med., 1911, iv, 498.

with complete heart-block. February 8, 1.30 P.M., complete heart-block still persisting; patient given two hypodermics of atropine. 5.30 P.M., incomplete block 3-1 rhythm. February 9, incomplete block 2-1 rhythm. February 10, 2-1 rhythm, alternating with normal rhythm. February 24, left University Hospital, not having had while there a single syncopal attack. March to May, seen at office, either 2-1 rhythm or normal rhythm. In May started to work as cabinetmaker again. May to October, worked. October 22, slight syncopal attack. October 25, syncopal attack, and patient was taken to Jefferson Hospital. October 26, had six to eight syncopal attacks. October 27, had four or five attacks. Refused to stay longer in hospital, and went home. October 28, one attack; admitted again to Jefferson Hospital; discharged next day. October 30, had four syncopal attacks. December 5, the patient came to the University Hospital to see Dr. Pepper, who found him sitting in the waiting room. The man stood up, and told Dr. Pepper how glad he was to see him again. He suddenly grew pale, put his hand to his heart, fell over on a bench, and had a general convulsive attack, with unconsciousness. He had at first stertorous breathing followed by shallow breathing. In about a minute his radial pulse, which had been absent, returned and immediately the color came back to his face and he regained consciousness, and in a few minutes walked up to the ward, having been persuaded to stay for a while in the hospital. This was the first time we had seen him have a syncopal attack. His radial pulse on this second admission to Dr. Stengel's wards was 44, falling shortly to between 24 and 36.

December 6. Tracings showed complete block, or complete dissociation of auricular and ventricular action, and during the patient's stay in the hospital this persisted unfailingly. There were no syncopal attacks on this day. Atropine, which had during his first stay in the hospital apparently interrupted the complete block, changing it first to partial block and then to normal rhythm, had no beneficial effect.

December 7. The following notes were made by the resident physician, Dr. Sledge: Patient's pulse has continued to run at about the same rate. This morning he had an attack, and was watched by one of the nurses. His pulse stopped for a few seconds; respirations at first were slow and noisy; face remained flushed, and consciousness was not lost. Pulse returned rapid and fluttering, respirations came back to normal, and in two minutes pulse had slowed down to 20. Patient was much exhausted. At 11.30 today, while sitting down on patient's bed to take his blood pressure, he looked up at me and said, "I think I am going to have another spell." I reached for his wrist and felt only one beat of his pulse; he became very pallid, there was a general muscular spasm with twitching of his limbs, followed in less than a minute by opisthot-

onos. (His opisthotonos lasted about a minute, followed by relaxation and intermittent spasms of extremities; absolute relaxation occurred when respirations stopped). No heart sounds were audible from cessation of pulse to its return; after that they were distinct. Breathing became rapid at first and very noisy, beginning to become slower and less noisy at the expiration of one minute, stopping altogether at the end of four minutes from the beginning of his attack. After respiration stopped, the patient slowly became cyanosed (he had been pallid before), and the vessels of the neck were distended, and no venous pulsation could be detected; he lay in this condition for nearly three minutes, and was apparently dead. Artificial respiration was begun, with head hanging over side of bed, and with my finger over his radial artery; at the expiration of one minute, his radial pulse suddenly recurred, soft and running, and his face became very much flushed; artificial respirations were stopped and he continued to breathe, respirations being slow and shallow. In less than a minute he was perfectly conscious, and attempted to move in bed; pulse had slowed down to 20. On being asked how he felt, patient said that he was thoroughly exhausted. Flushing was quickly followed by pallor. I asked the patient why he told me that he thought that an attack was coming on, and he replied that everything had begun to appear black, and his vision was disappearing. One hour after the attack was over the patient expressed a wish to die, and said such an end could not be far off. The thought of these attacks is a great mental strain on him. Patient had another attack tonight at 9.45; pulse stopped for over three minutes; respirations did not cease, and recovery was very rapid.

December 8. Patient had another attack at 12.30 last night, with loss of consciousness, but no cessation of respiration; attention was called to him by his noisy breathing. Four minutes after the nurse reached his side the radial pulse returned. After the attack had subsided, the patient was very hysterical for half an hour, believing that he was near death. He was quieted by a small dose of morphine. Patient continued restless and nervous the rest of the night; this was especially marked at six, and again at eight o'clock this morning; at both of these times he thought an attack was coming on, but pulse did not stop, nor had he respiratory difficulty. At 12.30 today patient was given an injection of "606" by Dr. Longcope. Dr. Pepper made pulse tracings before and after the injection, but no change was noted. At 5.15 tonight patient had some respiratory difficulty for a few seconds; pulse did not stop, nor was consciousness lost.

December 9. Patient had a short attack this morning at two o'clock; another attack came on at 8.30, and lasted over four minutes from the time the nurse reached his side; artificial respiration was required. At 11.30 he had another attack that lasted six minutes; respirations and jugular pulse stopped; eyes showed mark-

edly dilated pupils; after this he was wildly hysterical for a half hour. Another attack occurred at 4.30 and lasted about six minutes; artificial respiration was required for nearly a minute; violent mania was present after return of pulse for fifteen minutes. Patient was taken home in the ambulance at his own request.

He had on arriving at his home another severe attack, while the resident physician who accompanied him was present, and then for seven weeks was entirely free from them, although we had told him that he would undoubtedly have them and that he would die within twenty-four hours after leaving the hospital. He was visited at his home every two or three days for seven weeks, tracings being made on each occasion by Dr. Pepper. On December 13, 1910, he showed an incomplete block with a 3-1 rhythm, and on December 22, 1910, an incomplete block with a 2-1 rhythm; but the rhythm never became normal, and with the exception of these two occasions there was always complete auriculoventricular dissociation. Just before Christmas, 1910, his wife gave birth to a healthy boy; but this excitement in the family brought on no syncopal attacks in our patient. This child showed a negative Wassermann, as did its mother, although the patient on two occasions had given a positive reaction himself. He remained in the house sleeping on a lounge and walking around the first floor, but not venturing on the street, and on February 1, 1911, having been much wrought up over the withdrawal of his weekly income from an insurance company he had three syncopal attacks in one day and died during the last one.

A partial autopsy was performed by Dr. Austin about eight hours after death, and the heart removed. It was found to be greatly distended with dark fluid blood, a large quantity running out on cutting the vessels. The right side was particularly distended, the auricles, although enlarged, were not so extremely distended in proportion to the ventricles. The valves were perfectly healthy, and no macroscopic change in the heart, aside from the dilatation, was found. During life the right border was more displaced than the left, and there had been always noted a long systolic murmur at the apex. The patient's fingers had become quite clubbed, and the nails curved during the last year.

AUTOPSY PROTOCOL. Subject is a fairly well-developed Italian, male, adult. Little panniculus adiposis is present; no edema; no scars. An incision was made along the middle of the sternum, the skin and muscle reflected, and the sternum removed in the usual manner. The abdominal viscera were not fully exposed, owing to restrictions under which the autopsy was conducted.

The pleural cavities were free from fluid; the lungs appeared normal. The pericardium was much distended, and on being opened contained 30 c.c. of clear fluid and a greatly distended heart. The cardiac distention was most marked on the right side.

On cutting through the vena cavæ the entire mediastinum filled quickly with fluid blood. The heart and four inches of the aorta were removed for study. Sections were taken for histological study from the liver and from the right kidney, which was lobulated and deeply congested.

The heart weighed 420 grams; epicardium was smooth and glistening; moderate amount of subepicardial fat. Blood in the cavities was almost entirely fluid. The myocardium was grossly normal. The left ventricular wall at the base was 14 mm. and the right ventricular wall 3 mm. thick. The endocardium was smooth, no lesion being visible in the region of the bundle of His or of the sino-auricular bundle. The valve orifices measured in circumference: tricuspid, 15 cm.; mitral, 10 cm.; pulmonic, 8 cm.; aortic, 6.5 cm. Valve leaflets were thin and pliable. The region of the sino-auricular and His bundles was preserved intact for serial sectioning. Sections were taken also from other portions of the myocardium. The aorta showed a few nodules apparently beneath an intact intima.

HISTOLOGICAL PROTOCOL. Autopsy No. 3559, '99, 12. Report by Dr. Austin. The following tissues were prepared and submitted for histological examination: Heart, aorta, liver, kidney.

Heart: Sections through myocardium and endocardium show ventricular muscle fibers well developed. Nuclei stain normally. Striations are distinct. Throughout the sections there is a moderate diffuse fibrosis, which around some of the larger vessels is quite marked. The arteries show thickening of their adventitia. The endocardium is normal. The vessels are moderately filled with blood.

Sino-auricular bundle of Keith-Flack: Several transverse sections were made through this bundle and stained with hematoxylin and eosin and with Mallory's connective-tissue stain. The muscle fibers of the bundle appear well developed. There is considerable interstitial tissue in the bundle, not, however, an amount that can be considered excessive, the connective tissue forming a considerably less conspicuous feature of the cross-section than does the muscle tissue.

The bundle of His: The bundle was examined by serial longitudinal sections and stained with hematoxylin and eosin and with Mallory's connective-tissue stain. The course of the bundle was followed from Tawara's node to just beyond its bifurcation as an unbroken bundle, about 5 mm. in width. The course of the bundle is somewhat S-shaped. The muscle fibers of the bundle are slender and very closely approximated, with little interstitial tissue. The nuclei stain well. The cytoplasm shows distinct striation.

Aorta: Section shows nodular fibrous thickening of the deeper portion of the intima and fibrosis of the inner layers of the media. Musculature of the remainder of the media is well preserved.

Liver: Section shows a normal capsule. The lobules are distinctly demarcated. Immediately around the bile ducts there is a moderate fibrosis, with round-cell infiltration. The bile ducts show normal mucosa. The parenchymatous cells are small and well defined. Their nuclei stain well. In a few of these cells one or two small fat vacuoles are seen. Throughout the lobules the cells show a moderate deposit of intracellular, pale yellow, amorphous pigment. The capillaries and the larger vessels contain little blood.

Kidney: Section shows a thin capsule. The glomerular tufts are large filling the capsules, and show moderate congestion; otherwise normal. Tubular epithelium shows well defined finely granular cells; nuclei are well stained. In a few of the convoluted tubules the epithelial cells appear moderately swollen. In some of the lumens is a little granular or homogeneous material. The tubules are in close apposition and there is but little interstitial tissue. Throughout cortex and medulla is marked congestion, without pigmentation. *Treponema pallidum* could not be demonstrated in the liver, kidney, or aorta by the Levaditi method.

CONCLUSIONS. The special points of interest in this case, in addition to those noted in the first report,⁸ that we wish to bring out in this paper are:

1. That we have here a progressing typical case of heart-block lasting for three or four years, at first partial block alternating with normal rhythm, with occasional attacks of complete block, and later persistent complete block, and yet at the autopsy apparently no sufficient lesion was discovered in the bundle of His to explain the block.

2. The giving of a dose of "606" to the patient while he had complete heart-block and was having attacks daily of Stokes-Adams syndrome without any noticeable good or bad result.

3. We wish to call attention to the extreme length of several of the syncopal attacks. One attack timed by Dr. Sledge, the resident physician, lasted eight minutes, during the last four minutes of which the auricles apparently stopped beating in addition to the cessation of the ventricles. Apparently the man was dead, but artificial respiration brought him to life. Another attack witnessed by Drs. Edsall, Longcope, Sledge, and Pepper, and a number of medical students, was nearly as long, and very dramatic. This lasted six minutes, and for fully three minutes the auricles had apparently stopped beating, as no sounds could be heard over the chest, no pulsation noted in the neck, no respiratory movements occurred, and the patient's color, which at first had been white, became dusky. We all thought the man dead except Dr. Sledge, who, with some assurance on account of his previous

⁸ AMER. JOUR. MED. SCI., October, 1910.

success, began artificial respiration, and again restored the man to life and consciousness, which was promptly followed by a violent hysterical outburst, in which the man sang, cried, and shouted, and though none of us understood much Italian, we frequently heard the words "La morte" uttered with the most blood-curdling clearness. That these periods of apparent cessation of auricular action may have been due to auricular fibrillation cannot be denied.

4. In the first report of this case, already referred to, attention was particularly called to what was believed to be a genuine instance, though an isolated single one, of hemisystole. Apparently, as shown by the tracing on a single occasion, the left ventricle did contract normally after the auricular contraction; but the right ventricle did not contract, or possibly contracted very feebly, and the following statement was made in that article: "Probably it would be unwise, from this single observation, to say that in this particular case the division of the bundle of His going to the right ventricle was more involved or damaged than the division going to the left ventricle; but if further similar findings had been noted possibly such a localization could have been made."

The serial sections showed at the bifurcation of the bundle the branch passing to the right ventricle slightly encroached upon by an area of fat and fibrous tissue, while the branch to the left ventricle was normal.

It is, of course, difficult if not really impossible to properly interpret the concurrence of the single hemisystole and the slight lesion of the right branch of the bundle of His, if lesion it was. No other hemisystoles were noted, and the slight encroachment on the right branch of the bundle was not more than is sometimes found in apparently normal hearts.

5. It is interesting to note the occurrence of clubbed fingers in this case without any valvular disease of the heart or pulmonary disease.

6. That although during the man's first stay in the University Hospital he showed for several days constant irregular ventricular action during complete block without syncopal attacks, he never showed this irregularity later, even though he had syncopal attacks and complete block.

CLINICAL OBSERVATIONS OF REFLEX VAGUS PHENOMENA GROUPED IN SYMPTOM COMPLEXES.¹

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It is a well-known physiological fact that nerve impulses may reflexly produce the most diverse results, such as glandular secretion, regulation of blood supply, sweating, and muscular contraction; yet the role that nerve irritations and abnormal nerve impulses play in the production of reflex symptoms and the significance of such impulses in the elucidation of symptom complexes has not received the attention its importance warrants. In this paper I shall deal only with so-called functional disturbances of vagus impulses, both excitator and inhibitory in character, and shall exclude all organic affections that influence the pneumogastric. Before proceeding with the study of the clinical cases of vagus excitation, I shall briefly survey some facts in connection with the significance of the vagus in certain symptom complexes, and offer some general considerations on the subject of reflexes and the radiation of impulses.

Von Noorden² was the first to group symptoms resulting from irritations of the vagus. He confined his observations to purely hysterical cases ("hysterical vagoneuroses") presenting heart irregularities and hyperesthesia or anesthesia of throat and larynx. In describing a number of cases, he stated "if for any reason (organic stomach disease or nervous dyspepsia) hysterical people have gastric symptoms, functional disturbances of the vagi are common." Gowers³ described "vagal attacks" which consist mainly of subjective symptoms, gastric, respiratory, cardiac, or vasomotor in nature, the latter causing constriction of vessels and coldness particularly of the extremities. He believed these attacks usually occurred as epileptic equivalents.

Meltzer⁴ has done pioneer work in this country in directing attention to the clinical importance of the inhibitory nerves in both normal and pathological states; he ascribed several diseases of clinical importance (for example, cardiospasm, "icterus emotif") to disturbance of the function of inhibition. He believes that "an impulse which causes inhibition in a centre extending to a special function irradiates, spreads from there to other centres, and functions neither automatically nor physiologically connected with the primary centre." To quote from another part of the communication by the same author: "We learn that between the antagonists

¹ Read at the meeting of the Harlem Medical Association, New York, December 6, 1911.

² *Charité Annalen*, xviii, 249.

³ *Grenzgebiete der Epilepsie*, etc., 1908.

⁴ *New York Med. Jour.*, May 13, 20, 27, 1899; *Medical Record*, June 7, 1902.

(vagus and sympathetic) it is often practically the effect of only one force which is manifest during stimulation, and that it is neither always inhibition nor always excitation which is more favored by the stimulus."

It is, however, mainly due to the recent excellent clinical and experimental studies of Eppinger and Hess⁵ upon the condition they have termed "vagotonia" that distinct progress in the clinical study of vagus excitation and inhibition has been made. They have borrowed the term "vagal tone or vagotonia" from experimental physiology, where it has long been used, and have applied it clinically to those in whom the vagus system is particularly irritable and susceptible to stimulation and inhibition, and in whom certain vagotropic drugs, mainly atropine and pilocarpine, have respectively marked inhibitory and excitive (tonic) effects.

After dividing the nervous system into the animal and vegetative, Eppinger and Hess subdivide the vegetative into the sympathetic and the autonomous or system of the "enlarged vagus" ("erweiterte vagus"). Sympathetic and vagus nerve actions are antagonistic, the autonomous vagus impulses tending not only to antagonize but to partially paralyze the former. In connection with the cases to be described, it is of interest that these observers indicate that vagus irritations may produce active gastric peristalsis and even vomiting, and that the crises of many infectious diseases are coincident with profuse perspiration and cold extremities—both due to irregular blood distribution from disturbance of the vasomotor system. In many instances the above authors have succeeded in differentiating pharmacologically the two systems, sympathetic and vagus; for example, adrenalin irritates and excites only the sympathetic system, while atropine, pilocarpine, physostigmine, and muscarine have an elective action on the vagus system. Of these latter drugs, atropine often nullifies the effects of vagus stimulation, and hence partly antagonizes the action of muscarine, pilocarpine, and physostigmine.

A word in reference to the spread or radiation of impulses from one centre to another. Mackenzie⁶ states that abnormal stimuli of the sympathetic centres in the cord may spread beyond it and affect cells in the immediate neighborhood. Furthermore, according to Nagel⁷ there exists spinal as well as central impulse radiation. He quotes Heads' theory of spinal segmentation in skin hyperesthesia to prove spinal radiation of impulses.

I shall employ the term vagus excitation in the study of my cases, because, except for the marked salutary effect of atropine and the extreme vagus irritability in illness, the patients did not show when

⁵ Zeit. f. klin. Med., 1909, vi and vii, 345; lxxiii, 205, Sammlung klinische Abhandlungen über Pathologie und Therapie des Stoffwechsels und Ernährungsstörungen, p. 9.

⁶ Diseases of the Heart, second edition, p. 33.

⁷ Handbuch der Physiologie des Menschen, iv, 290.

normal any of the signs of "vagotonic disposition" described by Eppinger and Hess, namely, a tendency to perspiration, flushed face, moist skin, enlarged tonsils, slow pulse, frequent eructations, and generally increased reflexes. It may be that in some individuals the "vagotonic disposition" is not evidenced until strong abnormal excitation stimuli are present.

Some of the patients to be presented were "neurotic" in the ordinary acceptance of the term; in not a single instance, however, were there any hysterical stigmata.

Before proceeding with the clinical presentation, I wish to devote a few lines to the anatomy and physiology of the pneumogastric. The vagi originate in the nuclei in the lower part of the floor of the fourth ventricle, leave the skull through the jugular foramen and descend vertically to the root of the neck. Each vagus then descends along the esophagus, perforates the diaphragm, and spreads over the surface of the stomach. Filaments from the latter portion of the nerve anastomose with the solar, celiac, splenic, and hepatic plexuses of the sympathetic system. In the neck the main branches of the vagi supply the pharynx, esophagus, and larynx. In the thorax, the main branches are those that help to form the pulmonary and the cardiac plexuses. The cardiac branches anastomose⁸ with the cardiac branches of the sympathetic and form the deep and superficial cardiac plexuses innervating the heart.

According to the most recent studies, cardiac tissue possesses the functions of rhythmicity, excitability, conductivity, contractility, and probably tonicity. Most of these functions are profoundly influenced and inhibited by vagal stimulation.⁹ Upon the distal ends of the pneumogastric, peripheral stimulation of the corresponding branches of the vagus produces increased salivation (chorda tympani), contraction of pharynx and cardia, "gastric hypersecretion with or without hyperacidity, increased violent gastric peristalsis, which may easily lead to atypical (retrograde) peristalsis and even vomiting." (Eppinger and Hess.) Regarding the nervous mechanism and cause of peristalsis in the small intestine, the effect of the vagus is complicated not only by the action of the sympathetic (splanchnic nerves), but also by the automatic action of the Auerbach and Meissner plexuses. It is definitely known, however, that increased vagus excitability may give rise to abnormal tonic peristalsis of the small intestine. I shall not further enter into the effects of vagus stimulation on the musculature of the gall-bladder, on the pancreatic ducts, the lower colon and rectum, the genital organs and the blood, except to state that the vagus also affects all these organs, and in the blood, according to Eppinger and Hess, produces cosinophilia.

⁸ Dogiel-Pflueger's Arch. f. gesammte Physiologie, September, 1911.

⁹ Gaskell, Jour. Phys., 1886, vii, 1; Mackenzie, Diseases of the Heart, 1908, p. 7; Nagel, Handbuch der Physiologie des Menschen, i, 260.

From the above we observe that throughout its long course the vagus sends branches to many important structures and is directly concerned with many vital processes; *a priore*, then, it can be readily seen that abnormal peripheral irritation in one end organ may produce diverse reflex results not only in adjoining, but also in remote parts of the body.

I now wish to describe a series of cases, eight in all, which, of many that I have seen, have particularly and strikingly impressed me as showing the importance of abnormal irritation of the vagus in various clinical conditions. Some of these observations were made in patients with organs already the seat of pathological change; in these the added vagus irritation had a particularly marked effect upon the symptoms present.

CASE I.—W. D., aged twelve years, a strong, healthy boy. A general physical examination made several weeks before his present illness, was entirely negative. The boy's illness consisted of an attack of influenza (bronchitis) with two relapses (mild coryza, mild eustachitis). Each attack began with a temperature of 102°, lasted about four days, and ended in a mild crisis, accompanied by vomiting, sweating, and an irregular pulse. The pulse dropped from 80 to 50, caused by varyingly long pauses between the beats both at apex and wrist. No polygraphic tracings were made so that the exact nature of the irregularity could not be determined; it was probably, however, of the type described by Mackenzie¹⁰ as sinus irregularity and commonly ascribed to the effect of vagus inhibition on the normal rhythm. There was absolutely no sign of any heart disease present—no decompensation, no murmurs, no dyspnea, no edema. Except at the time of the crisis, the patient felt absolutely well.

The features of this case which point toward vagal influence are the events occurring at the crisis: (1) The irregular pulse; (2) the vomiting; (3) the sweats.

1. *Irregular Pulse.* The influence of the vagus on the normal sinus rhythm has already been mentioned. An interesting phenomenon in conjunction with the irregularity was that forced rapid breathing a few times always overcame the sinus irregularity; the pulse became regular and remained so for a few minutes. The explanation of this phenomenon appears to me to be as follows: normal rapid impulses originating in the vagal pulmonary plexuses temporarily overcame the disturbing effect of the influenza toxin on the vagus centre and thus temporarily produced a rhythmical pulse.

2. *Vomiting.* It is well known that vomiting can be readily produced by central vagus disturbance. In this patient the toxemia

¹⁰ Diseases of the Heart, 2d ed., p. 141.

acted upon the vagus centre and, irritating the gastric filaments, caused peristalsis and emesis.

3. *Sweating.* This is, of course, an almost invariable symptom of fever crises. It is here mentioned on account of its connection with the symptoms of vagus excitation. Because of the effect of atropine (vagotropic), Eppinger and Hess have determined, that despite generally accepted physiological and anatomical conclusions, sweating is under the influence of the vagus system and not of the sympathetic. It appears to me, however, that the critical sweats are due to the radiation of the impulses from the vagus centre to the sympathetic system.

Crises such as above described are quite common, particularly in febrile affections, but sufficient emphasis has not been placed upon their cause. I would suggest the name vago-excitor crisis for such a symptom-complex. Further reference will subsequently be made to this condition.

CASE II.—Mrs. F., aged sixty years; myocarditis and marked arteriosclerosis. In June, 1910, she had an influenzal pneumonia that involved three different lobes of the lung (pneumonia migrans). Each pneumonic involvement, lasting five days, ended in a very sharp crisis: extreme prostration, sweating, severe retching and vomiting, and extremely irregular and tumultuous heart action (so-called delirium cordis). The irregularity consisted in complete arrhythmia, the beats followed no rhythm, the rate varied momentarily between 60 and 160, strong and weak impulses following each other in a haphazard manner.

Despite arrhythmia and the pulmonary involvement there was no dyspnea and no pulmonary edema. Between the crises and during the course of the pneumonia the pulse was usually regular and of good quality. A distinct herpes labialis et nasalis accompanied each crisis. After the pneumonia there was, for some weeks, edema of the legs and an occasionally irregular pulse.

CASE III.—G. R., aged forty-three years, nephew of Case II, had never been previously ill. In 1910 he had a grippe pneumonia, involving in succession five different areas of the lung (pneumonia migrans). The breathing remained 28 to 36 per minute throughout his illness. At the end of each pneumonic process there was a crisis, with sweating and nausea, the temperature dropped from 105° to $100\frac{1}{2}^{\circ}$. With each new pneumonic involvement, and usually two to four hours before audible physical signs were present, the pulse became exceedingly irregular, exactly as in Case II. With it all the patient was conscious: there were no cold extremities, no dyspnea, no edema of the lungs, no decompensation. When physical signs of a new involvement became evident the cardiac irregularity disappeared. The patient entirely recovered and no signs of any heart irregularity remained.

Grouping Cases II and III, we again have examples of marked

vago-excitor crises, the influenza toxin—more severe than in Case I—not only inhibiting heart action, but temporarily paralyzing the vagus centre, thus producing very pronounced arrhythmia.

It appears illogical to me to ascribe the cardiac irregularities accompanying in the one case each pulmonary crisis, and in the other, each new pulmonary involvement, to a fresh myocarditis lasting from minutes to hours and then disappearing, leaving no permanent trace. On the other hand, it is well known that toxemias do involve nerve structures and end organs. Furthermore, the more prominent symptoms of acute myocarditis—dyspnea, edema of the lungs, cyanosis, etc.—were absent, despite the active and widespread pneumonia.

Despite their apparent gravity, conceiving the cardiac irregularities in these three cases as part of a vagus symptom-complex and mainly functional, I was able to give a good prognosis in each case.

CASE IV.—Mrs. H., aged fifty years; is passing through the menopause. Except for "rheumatism" of the legs, she had always been well. Three years ago, without other apparent cause, twenty-four hours after a death in the family, she suddenly developed extremely severe epigastric pains and sensitiveness; with exacerbations and remissions, this pain lasted for months. There were oft-repeated hunger pains both day and night. Acids even in minute amounts increased the gastric distress. There was no difficulty in swallowing. Abdominal examination showed the stomach outline to be small; at times the whole epigastrium felt as if it were occupied by a smooth, globular, semisolid mass. At such times, though abdominal pressure was painful, it was immediately accompanied by loud, explosive, continued eructations of gas having no odor or taste; these eructations sometimes lasted a half hour and were followed by temporary relief from pain. Repeated observation shows that there is apparently no air swallowing. After six months of the above symptoms, examinations of the fasting stomach showed no gastric juice or stagnant stomach contents. Upon one examination there was fresh blood on the end of the stomach tube. One-half hour after an Ewald test meal, very little stomach contents remained: examination showed it to be well digested: total acidity, 70; free HCl, 25; no lactic acid. After three days of meat-free diet there was no occult blood in the feces. During the next few months the symptoms were somewhat different in character. There were occasional acid eructations and vomiting of sour fluids in the morning. The patient complained of boring pains high up in the epigastrium, increased on pressure. There was a marked zone of skin hyperesthesia (Head's zone) corresponding to the stomach; this zone was present for a number of weeks. Several times, despite extreme care in diet, there were very sudden explosive attacks of diarrhea and vomiting. The patient frequently had cold feet and

cold, blanched hands. She also complained of palpitation, though the heart beat was not rapid nor irregular. During one year the patient lost forty pounds in weight. Under the routine treatment for ulcer (rest in bed, alkalies, diet, etc.) and the addition of atropine, the patient gradually improved. Since the above symptoms subsided the patient has occasional attacks of mild epigastric distress and eructations. There has been a gradual increase in weight.

The salient features of this case are: (1) Acute onset after shock; (2) spasmodic contractions of stomach wall and disturbed gastric secretion; (3) after some months, the probable development of an ulcer. The details of this case will be discussed in conjunction with the following:

CASE V.¹¹—Mrs. C., aged forty-four years, mother of three children, had always been absolutely well. Ten years ago she witnessed an accident—a man fell from a window and was killed before her eyes. She was profoundly shocked by the accident, and that *same night* developed severe epigastric pains. The patient remained in bed for six weeks, suffering from continued, intense boring pains in the epigastrium radiating to the spine between the angles of the scapulæ, vomiting of sour fluids and masses, retching and palpitation accompanied by a tingling sensation in the seventh left interspace. These symptoms were present by night as well as by day. Since that time, during all these years, the patient's symptoms have continued, so that for periods of weeks, when pains or vomiting were particularly severe, she had to remain in bed. In addition to the initial symptoms, there were frequent attacks of very severe epigastric pains, followed and temporarily relieved by loud, explosive eructations lasting several minutes; of sudden choking sensations, during which she could swallow only fluids; of frequent dizziness; of attacks of constipation, in which the bowels moved only once a week; of marked epigastric hyperesthesia. The patient lost 35 pounds in weight; she subsisted mainly upon bread and butter. One year ago the gastric symptoms—nausea, vomiting, and pain—again became acute. The diagnosis of gastric ulcer and pyloric stenosis was made. She was operated upon, the ulcer excised and a posterior gastro-enterostomy was done.

Immediate post-operative course. The temperature was normal throughout, there were no signs of peritonitis or wound infection. Her bowels moved the second day after operation and daily thereafter. For one week there was constant intractable vomiting and hiccough, the pulse was irregular and dropped to 50. Finally the stomach became more tolerant, the vomiting and singultus ceased, the pulse became regular. After one year the patient gained 15 pounds, and at the present time has excellent appetite and digestion.

¹¹ I am indebted to Dr. E. Adams of New York, who operated upon her, for his permission to study and publish this case.

The important features of this case are : (1) Onset immediately after shock; (2) gradual development of a gastric ulcer; (3) post-operative symptoms due to exceedingly powerful vagus and phrenic excitation.

Before proceeding with an analysis of Cases IV and V, we must for a moment digress to briefly consider the important theories and experimental work on the etiology of gastric ulcer.

Vagotomy¹² has been the operation most recently employed in the experimental production of gastric ulcer. Kawamura reviewed the work in this field; performed a considerable number of vagotomies in rabbits and dogs, and has made a careful study of the pathological findings and of the stomach contents in his series of cases. Although his results are by no means uniform, it may be definitely stated that in many rabbits (27 out of 37) gastric ulcer followed the division of the vagi.

The theories that have been held upon the etiology of ulcer are varied. Virchow believed the cause to be local circulatory disturbances, thromboses, or hemorrhagic erosions, the normal neutralization of the acid gastric juice by the blood not taking place. According to Payr,¹³ retrograde hemorrhagic infarcts are responsible for the fundamental changes that lead to ulcer. Diminished alkalinity of the blood (Pavy), compression of the mucosa in the folds of the gastric mucous membrane with resultant erosions are other theories. Grouping more recent opinions Ewald¹⁴ states that the most important factor is the hyperacid gastric juice acting upon circumscribed areas of altered mucosa (of mechanical, chemical, thermal, vascular or infectious origin). Thus the fundamental cause of gastric ulcer remains unknown.

Returning to a consideration of Cases IV and V, it appears to me that these two instances conclusively prove that intense functional nervous influences—shock—may, by powerful excitation of the vagi, produce a primary gastric neurosis and consequent disturbances of gastric secretion, and possibly, also, produce disturbed gastric circulation, and finally result in the formation of an ulcer.¹⁵ The acute gastric symptoms immediately followed the mental shock which our two patients underwent; in fact, the march of symptoms dated from the moment of the psychical disturbance. In addition, Case V indicates well an extreme sensitiveness to vagus influences. Persistent vomiting and disturbed heart action (slow pulse) followed the operation of excision of the ulcer. It appears to me that these symptoms were due to the irritation of the gastric vagus branches from the necessary manipulations of the operation as well as to the

¹² Zironi, *La Riforma Medica*, 1906, xv, 395; Von Yzeren, *Zeit. f. klin. Med.*, 1901, xliii, 181; Gibelli, *Archives Internationales de Chirurgie*, 1908, iv, fase. 2.; Donati, *Centralblatt f. Chirurgie*, 1904, p. 346; Kawamura, *Deut. Zeit. f. Chir.*, cix, H. 5, 6, May, 1911.

¹³ *Arch. f. klin. Chir.*, 1907, lxxiv, 799.

¹⁴ *Modern Clinical Medicine*, 1906.

¹⁵ *Stockton New York Med. Jour.*, October 30, 1909.

unavoidable division of the many small branches of the nerves. The singultus was caused by reflex disturbance of the phrenic from irritation of the solar plexus to which it sends branches.

The pronounced effect of atropine in Case IV is of interest. Although atropine has been administered to this patient for more than a year, very minute doses ($\frac{1}{800}$ of a grain) continue to control the gastric symptoms.

CASE VI.—Mrs. B., aged eighty years. She is quite stout and has a slight fatty myocarditis; no apparent arteriosclerosis. One year ago she suffered from left-sided kidney colic and pyelitis. After several days a stone was passed. The pyelitis, accompanied by remissions and temperatures, lasted over two months. Soon after the fever subsided there developed severe bilateral intercostal neuritis, with extreme hyperesthesia in the corresponding intercostal spaces at the intercostal nerve exits. During the attacks of neuritis (which lasted intermittently for months) one or more of the following symptoms suddenly appeared: choking sensations, pains in the gums, spasmodic cough, either during the day or at night, difficulty (though no pain) in swallowing, sudden vomiting of solid and liquid food often immediately after they were swallowed, expectoration of large quantities of pure saliva occasionally awakening her from sleep. These different attacks were usually accompanied by exacerbations of the neuritis. Throat, esophagus, lungs, and kidneys were normal. Except for the neuralgic intercostal pain and the attacks above described the patient was in excellent general health.

That the intercostal neuritis was due to the septic pyelitis is evident, and it appears unquestionable to me that abnormal impulses from the intercostal nerves, passing through the spinal cord, affected the vagus centre and thereby caused the various vagal irritative symptoms described—laryngeal, pharyngeal, esophageal and gastric spasms, and salivary hypersecretion.

CASE VII.—Mrs. R., aged sixty-nine years, has marked arteriosclerosis, myocarditis, and splanchnoptosis. Except when ill from any cause, her pulse is regular. Two years ago, after a vaginal hysterectomy for uterine tumor, there were several severe attacks of vomiting, with irregular heart action. About one year ago, following worry over the illness of her son, she had a very sharp attack of acute gastric dilatation. The temperature was 100.4°. The pulse and heart, until that time only occasionally arrhythmic, now became very irregular. There was no dyspnea, no decompensation. With lessening of the gastric symptoms the heart became more regular and only occasionally intermittent. Two months after the attack the heart was still irregular, and for the first time there were signs of heart failure: dyspnea, cough, and slight edema of the legs. Examination of the arterial and venous pulse by means of polygraphic tracings shows so-called complete irregularity of the

pulse (auricular fibrillation). Following the attack, the patient suffered for months from intercostal and abdominal neuralgias, with superficial and deep hyperesthesia, in the corresponding regions. There was also one very severe attack of constant belching, lasting about one half hour without any apparent cause.

Comparison with Case VI shows the reflex arc through the spinal cord exactly reversed. Here vagus excitation resulting from acute gastric dilatation affected not only the heart, but also reflexly the intercostal and abdominal nerves, with resultant neuralgias. The belching was due to sudden excitation of the gastric vagus filaments, producing spasmodic contraction of the stomach.

CASE VIII.—A. S., peddler, aged twenty-nine years. Drinks ten cups of tea daily. History otherwise negative. A year and a half ago, without apparent cause, he suffered from ptyalism, which frequently disturbed his sleep. There was no cough, no bronchial symptoms, no pharyngitis. After several months the above symptoms were partly replaced by choking sensations, usually present in the morning, and by frequent explosive belching attacks particularly after breakfast. He was often awakened from sleep by sensations of hunger and by intestinal rumbling. Subsequently he complained of palpitation and of "uneasiness" in the chest. Examination of the heart showed it to be of normal size; heart's action is rapid, regular, a soft systolic murmur accompanies the first sound. Examination was otherwise entirely negative.

This patient shows the vago-excitor phenomena in the ptyalism, the pharyngeal spasms, belching, and hungry sensation (gastric irritability). The rapid heart action and resultant slight cardiac dilatation and systolic murmur, I attribute to a reflex disturbance of the sympathetic, thus allowing unrestrained action of the cardiac accelerators.

The tea drinking is the only factor in the patient's history which points to an etiology for the vagus excitation.

It will have been noted that some of the statements I have made are based on purely theoretical grounds. This is unfortunately necessary since we are not as yet in possession of sufficient facts in connection with functional affections of the vagus or indeed of other nerves. By careful analysis of the less obvious symptoms of a series of cases I have attempted to correlate, to group together under a single condition many symptoms that have heretofore been unclassified, and to show the inter-dependence of apparently disjointed phenomena.

As also stated by Eppinger and Hess, it is possible that cases showing a marked susceptibility to vagal influences follow a familial type. Three of the cases here reported were two sisters and a son of one of them; two cases were mother and daughter. My observations, however, do not comprise sufficient cases to warrant any definite deductions.

In conclusion, I would state:

1. The study of reflex phenomena is of great importance with reference to vagus excitation.

2. In some instances of gastric affections and of heart irregularities, a careful survey of the clinical picture and a search for apparently minor symptoms will reveal the significance of vagus excitation in the symptom-complex.

3. The discovery of such a symptom-complex is of special importance in prognosis and therapeusis.

4. Gastric ulcers may occasionally originate from functional vagus excitation.

5. Some apparently hysterical symptoms will be found to be functional (vago-excitve) and not neurotic in the ordinary sense of the word.

REVIEWS

AMERICAN PRACTICE OF SURGERY. EDITORS, JOSEPH D. BRYANT, M.D., LL.D., and ALBERT H. BUCK, M.D., of New York City. In eight volumes. Vol. VIII. Pp. 1146, with 406 illustrations. New York: William Wood & Co., 1911.

THIS is the last of a series of eight ponderous volumes comprising, in the words of the title page, "a complete system of the science and art of surgery, by representative surgeons of the United States and Canada." The first volume was reviewed in these columns only five years ago; and when the magnitude of the undertaking is considered, it is truly remarkable that it has been possible to complete the series in so comparatively short a time. •

The present volume concludes regional surgery, comprising articles on intrathoracic surgery, by Joseph Ransohoff and J. Louis Ransohoff, of Cincinnati; surgery of the spleen, by Alex. E. Garrow, of Montreal; surgery of the kidneys and ureters, by James Bell, of Montreal; surgery of the pancreas, liver, gall-bladder and bile ducts, by Geo. D. Stewart, of New York City; that of the urinary bladder and prostate, by Alex. Hugh Ferguson, of Chicago; of the ovaries and Fallopian tubes, by Benjamin R. Schenck, of Detroit; of the uterus and its ligaments, by John B. Murphy and Frank W. Lynch, of Chicago; extra-uterine pregnancy, Cæsarean section, etc., by Lewis S. McMurtry, of Louisville; together with disquisitions on surgery and the law, by Stephen Smith of New York, and Sidney Smith, of the New York bar; on hospitals and hospital management, by Christian R. Holmes, of Cincinnati; military surgery, by Major Charles Lynch, United States Army; naval surgery, by Surgeon-General Charles F. Stokes, United States Navy; administrative railroad surgery, by James Alexander Hutchison, of Montreal; together with a brief appendix on the relation of blood pressure to surgery, by J. E. Sweet, of Philadelphia. There is also a general index to the entire eight volumes. This appears to have been constructed by a mechanic rather than a surgeon, and combines all the faults of the indices to the preceding volumes.

The article on intrathoracic surgery, as explained by the editors in a footnote, was not completed in sufficient time to be included in its appropriate place in Vol. VII; but it appears, nevertheless, to

have left the authors' hands too soon for them to make any mention of the method of anesthesia by "intratracheal insufflation," which bids fair to supplant the methods of "differential pressure." As this is the most notable advance in intrathoracic surgery during the past decade, it is a pity that it was overlooked. Brought prominently before the profession by Meltzer and Auer in 1909, it may be said to have become well recognized by the end of the year 1910. The article includes, besides surgery of the lung and mediastina (exclusive of the heart), some mention also of intrathoracic (aortic and innominate) aneurysms. This is well, as the monograph by LeConte and Stewart, in Vol. VII, does not discuss the individual forms of aneurysm; indeed, nowhere in the entire system can there be found any account of subclavian, popliteal, or other of the more important varieties. Carotid aneurysm is dismissed in a few lines in the article on the surgery of the neck, in Vol. VI.

In the otherwise admirable discussion of the surgery of the kidney and ureters, by Bell, one likewise looks in vain for any mention of acute septic infarct of the kidney, made so familiar a subject by the teaching of Brewer, of New York. Bell thinks renal tuberculosis usually primary in the kidney, and he advises nephrectomy when the patient is seen in the operable stage.

The contributions of Geo. D. Stewart, on the surgery of the pancreas, liver, and bile passages, call for little comment. They are sensible; and they form a safe guide for a surgeon who wishes to be neither hysterically radical nor hopelessly wedded to conservatism. On the subject of the pathogenesis, however, his views are not in accord with current teaching; he holds that most infections of the bile passages ascend the ducts from the intestine; he dismisses infection by way of the portal blood stream with a mere mention, and thinks the systemic circulation a very rare channel; and he successfully evades a discussion of the pathogenesis of pancreatic infections.

The late Alexander Hugh Ferguson lived to complete a characteristically positive and personal article of one hundred and twenty pages on the bladder and prostate. He has made much use of Deaver's monograph, both in text and illustrations, but perhaps with too little credit. He condemns all operations for prostatic carcinoma, except the establishment of a suprapubic fistula by Hunter McGuire's method. While he prefers the perineal route for prostatectomy, he generously quotes, *verbatim*, at a length of over seven pages Mr. Freyer's own account of his method of suprapubic prostatectomy; and damns the Johns Hopkins operation, not so much with faint praise (for praise is absent from his lips), but by the assertion that the "conservative" feature of it "does not appeal to decent old men."

The subject of abdominal gynecology covers 320 pages, of which

by far the largest part (245 pages), written by John B. Murphy and Frank W. Lynch, is devoted to the surgery of the uterus and its ligaments. This is a very thorough article, but not so comprehensive as could be wished. Especially valuable is the discussion of uterine carcinoma; the authors approve the modified Wertheim operation, in "operable cases," and express their conviction of the value of the cautery and of chloride of zinc applications in those which are inoperable, which unfortunately in this country still form by far the larger class.

The monograph on surgery and the law is composed chiefly of court decisions, systematically arranged according to the legal questions involved, and should prove of great value to both lawyer and surgeon in preparation of medicolegal suits, expert testimony, etc.

Dr. Holmes, who is a member of the Building Commission of the New General Hospital in Cincinnati, has done the profession a distinct service in collecting so much valuable information as to hospital construction and management. He prefers the pavilion plan and urges that urban hospitals be established in suburban districts, or, at any rate, where there shall be plenty of air and light, with freedom from dust and noise; arguing that automobile ambulances, electric street cars, and other means of transportation render suburban points readily accessible for both patients and their friends. In this scheme, however, he fails to consider the requirements of hospital out-patients and accident cases, unless separate receiving stations are to be maintained in the thickly populated centres. No doubt the total abolishment of dispensaries would simultaneously abolish the "dispensary evil," but certainly it would work great hardship to the deserving poor, as well as to that large middle class, who, while they can afford to pay small fees, prefer to be reckoned among the paupers rather than receive the inefficient treatment which too often is all they can obtain outside of a hospital.

Reviewing these eight large volumes as a whole, it must be confessed that they scarcely fulfil the expectations of the subscribers. They are clumsy, both physically and intellectually. The paper is thick and brittle; the type is large, well leaded, and much unnecessary display typing is employed. By proper condensation of the merely physical attributes of the volumes their unwieldy size could be very materially reduced. The editing leaves much to be desired. To ascertain the author of any article in the entire system one must turn to the initial page of the article in question; then to ascertain who he is (for, unfortunately, many of the authors are not as truly "representative" as the title page suggests) one must turn again to the list of authors at the beginning of each volume. It surely would have been much better, and certainly very easy, to include in the table of contents both the

authors' names and their "credentials." It was quite needless to repeat the legend "American Practice of Surgery" at the top of each of the 7152 left-hand folios which the system contains; the subject of the special monograph should be stated here, and its subheadings on the right hand pages; there is no one who does not know how much more useful a volume is when thus arranged. These are clear faults of editing. Since the publication of the last volume the publishers have forwarded to the subscribers small slips of subject headings to be pasted on the backs of the volumes, thus adding greatly to the ease with which a given subject may be found; but there seems no reason why these headings should not have been printed on the backs of each volume as it issued from the press. For four years it was necessary, before finding the subject desired, to consult the index of each of the volumes published up to date.

The individual articles (one hundred and two in number) contained in these eight volumes are, as might well have been expected, of very varying importance and value. Some of the authors (fortunately not a majority) seem to have had no other object in view than to get through with their task with the least possible expenditure of energy and intellectual acumen; they have scribbled down a lot of ideas worthless alike from their lack of logical sequence and from their innate inanity; while others have gone at their task seriously and conscientiously, and have furnished in some instances brilliant, in all cases worthy, contributions to the science of surgery.

It is well at the conclusion of every endeavor, literary or other, to bear in mind two precepts: the first, that no matter how well the assigned task has been performed, the workers have done nothing but their duty, and that they are therefore "unprofitable servants;" the other, that well-known quotation from Seneca the Philosopher: *Multum restat adhuc operis; multumque restabit, nec ulli nato post mille sæcula præcludetur occasio aliquid adjiciendi.*

A. P. C. A.

THE LIFE HISTORY, FUNCTION AND INFLAMMATION OF THE APPENDIX. By EDRED M. CORNER, M.A., M.C., F.R.C.S., Surgeon to the Surgical Isolation Wards and Out-Patients, St. Thomas's Hospital Pp. 23. London: John Bale, Sons & Danielsson, Ltd., 1911.

THIS little volume is a reprint of an address delivered at the Clinical Society at Manchester, January, 1911. This address might have been interesting to a group of laymen but contains nothing new that would interest physicians. The first portion of the text is devoted to a discussion of the relation of bread, made

from flour rolled by big steam rollers of a fluted type, to the etiology of appendicitis. Corner does not, of course, believe that appendicitis is solely due to our daily bread, but does believe that since the introduction into England of American methods of preparing flour, appendicitis in that country is on the increase. One might remark that there are other reasons. The remainder of the booklet is devoted to a discussion of certain well-known facts, namely, the advisability of removing the appendix if diseased; the existence of "unconscious, undiagnosable, unrecognizable appendicitis," which perhaps is only our old friend appendicitis larvata; the gradual atrophy in most people after the age of twenty years of the lymphoid tissue of the appendix, a fact pointed out by Ribbert many, many years ago; finally, the increasing frequency with which carcinoma of the appendix is detected histologically.

Perhaps the contents of this book seem trite to an American for the reason that "in America it is very common, indeed, to have the appendix removed on a comparatively slight provocation." But, as a result of this rashness, we have learned long ago the facts which Mr. Corner now teaches.

G. P. M.

FOOD AND THE PRINCIPLES OF DIETETICS. By ROBERT HUTCHISON, M.D. (Edin.), F.R.C.P., Physician to the London Hospital, etc. Third Edition; pp. 615; 3 colored plates; 33 illustrations. New York: William Wood & Co., 1911.

A SERIES of lectures addressed to the students of the London Hospital formed the nucleus for the first edition of this work. The reception given these lectures and the almost total neglect of the subject of dietetics in ordinary medical education induced the author to publish them in book form. In recasting them for publication, however, a large amount of additional matter has been used. In the present edition the whole book has been thoroughly revised and the chapters dealing with the "Use of Diet in Disease" considerably enlarged. A new chapter has been added on certain "Dietetic Cures and Systems."

The work is thoroughly scientific and up to date, and the conclusions are based on the results of scientific research so far as they have been worked out at the present time. Much still remains unsolved in our ideas of the assimilation of food by the body in health and disease. At the present time of close inspection of proprietary foods the chapter devoted to "Artificial and Predigested Foods" is of particular interest, for the author has attempted to arrive at an unprejudiced estimation of their value.

The previous editions of the work have already held a prominent position among books of reference on this subject, and the present

volume promises to retain this place. The book is very readable and is of unusual interest in the way of general information about foods, even to lay readers. The typographical errors are few, the printing clear and distinct, and the index unusually full and complete, making reference to any of the numerous subjects easy. We can well recommend the book as an excellent work on the subjects of food and dietetics, and as such it will appeal not only to students and instructors in these special subjects, but should be of great help to physicians and students of medicine who wish to obtain the full benefit of food in the preservation of health or in the treatment of disease.

F. H. K.

ORTHOPEDIC SURGERY. By EDWARD H. BRADFORD, M.D., and ROBERT W. LOVETT, M.D. Pp. 410; 364 illustrations. New York: William Wood & Co., 1911.

THE present volume is much smaller than those issued by the same authors some years ago. It is an entirely new book. They present it as "a condensed handbook for the use of students and practitioners, embodying a brief statement of the generally accepted opinions as to the nature and treatment of the affections under consideration."

Viewed from their standpoint the book is certainly satisfactory. The subject is presented in a systematic, careful, and clear manner that cannot fail to be suitable for those who are to a great extent ignorant of this branch of surgery.

It seems to be most admirably suited for a students' text-book. Its conciseness, its brevity, and the clear, lucid descriptions and abundant illustrations all recommend it to that class. Students have not the time to study large treatises, or to go into the subject exhaustively. The time has passed when the subject of orthopedics can be adequately treated in works of general surgery. It is imperative that the student possess some such book as this and familiarize himself with its contents. When, however, the student enters upon the practice of medicine, some of the features that commend the book to the undergraduate tend to make it less satisfactory for the practitioner. The short, brief, concise, and didactic descriptions and directions are not sufficient for the physician, who wishes to thoroughly inform himself about an individual affection or class of cases. He should supplement it with a larger work, in which sufficient space is given to detailed explanations and directions.

The views expressed throughout the book are preëminently those of the Boston school of orthopedists, and though sound, are naturally conservative. To have presented more fully the operative or

more radical side of orthopedic surgery which is developing so rapidly would have been impossible without unduly enlarging the size of the book, and thereby impairing its value as a text-book.

It is stated that while synovial tuberculosis exists in a large majority of the cases the affection arises in the bone. In view of the deaths that have been caused by applying pure carbolic acid to the tissues, we think it would have been wiser to have omitted mention of its use in the operative treatment of hip disease. We doubt the advisability of Bardenheuer's excision of the acetabulum, even as a life-saving measure. We think it would be well to mention multiple cancellous exostosis, probably more common than myositis ossificans. The failure to recommend cod liver oil in rickets should be remedied. We fail to find any mention of the reviewer's method of reducing congenital luxations of the hip by placing the child on its face and pushing the head of the femur into place; thus is our vanity hurt. Nothing is said about the use of outside braces for club feet, perhaps this was intentional, but if so we must dissent. On page 355, fifth line from the bottom, the word "tendon" is used instead of "knife," and on page 203 "Diagnoses" occurs twice in large type.

In conclusion we commend the book thoroughly to the profession, and suggest that every general surgeon secure a copy and read it carefully, as thereby he will acquire a faint idea of what ought to be done for the too many cripples that are still in need of proper treatment.

G. G. D.

PUERPERAL INFECTION. By ARNOLD W. W. LEA, M.D., B.S., F.R.C.S., Lecturer in Obstetrics and Gynecology, the University, Manchester; Surgeon to the Northern Hospital for Women, Manchester. Pp. 384; 23 illustrations and 36 plates. London: Oxford University Press.

It is impossible to do justice to this work without seeming to flatter. No adverse criticism has any place. It is complete in grasp and definite in teaching, and, best of all, it is eminently sane. We believe that the above will be the verdict of those men whose experience has made them competent to form a judgment.

The author opens the work with a most interesting historical review, and then devotes a chapter to the classification of the various forms of sepsis. In accord with present-day teaching he classifies as toxemias all septic processes uncomplicated by deep penetration or blood invasion of organisms, whether or not said organisms are pathogenic or putrefactive.

The third chapter is concerned with the frequency, mortality, and morbidity of sepsis, and if there were nothing else of value to

commend the book, the compilation of this statistical chapter would make it worth while. Unfortunately the general mass of the profession, in whose hands lies the bulk of obstetrics, are prone to belittle both the bitter experience of the past and the scientific testimony of today, and, continuing to worship before the tablet of mercury in a dirty basin of unboiled water, still needlessly jeopardize human lives. This chapter should be read by every man engaged in this branch of medical work. In drawing his conclusions to this chapter the author gives three rules by which puerperal morbidity in obstetrics may be greatly reduced, namely, by the complete disinfection of those attending cases of labor, by efficient disinfection of the external genitalia during labor; by limiting the examinations so far as possible, and by the avoidance of all unnecessary operative interference. It would be well if the second of these rules could be branded upon the conscience of every one engaged in midwifery practice. Consulting experience teaches that there is a passable observance of the first and last of the three rules mentioned above, but that the majority of even intelligent men have no conception of adequate external cleansing, and, therefore, naturally cannot practice it.

The chapters upon bacteriology and etiology are up to date, and will well repay careful reading. Among other interesting questions discussed, perhaps the most interesting is whether pathogenic organisms may be found in the uterine cavity of normal cases at various intervals after delivery, and also that while auto-genetic infection is rare, as a cause of severe sepsis, its occurrence probably explains a number of cases of slight pyrexia in the early puerperium. This whole question is of the greatest interest, but as yet cannot be looked upon as at all definitely settled.

The chapters upon general pathology, pathological anatomy, and the symptoms of sepsis are the result of painstaking care in preparation. It gives particular pleasure to note that the relation between the polymorphonuclear and eosinophile cells is insisted upon as a prognostic sign of value in severe cases.

A separate chapter is devoted to localized infection of the generative tract, and in the next succeeding chapter the prophylaxis of infection is carefully elaborated under three subdivisions, namely, during pregnancy, during labor, and during the puerperium. While there is nothing new in this chapter there is a great deal which should be assimilated and practised, particularly by those men to whom obstetrics is but a small part of their daily work. In speaking of the use of gloves, however, there is one point which cannot be passed without adverse comment, namely, the statement that their use makes it difficult to detach membranes or portions of placenta from the uterine wall. To this the reviewer cannot subscribe, since a little perseverance will enable any one to become as expert with the gloved as with the bare hand. The increased

safety offered by their use in intra-uterine manipulations, which by the way is definitely stated on the succeeding page, should have excluded this objection.

In his consideration of the treatment of infected cases the author lays stress upon the fact that there is no specific, and calls attention to the results obtained by purely expectant handling. Isolation, rest, nutrition, and the use of rubber gloves are insisted upon as general principles.

It is interesting to note that *écouvillonnage*, or the use of the intra-uterine brush, is recommended as a valuable means of cleansing the uterine cavity. Good results from this method are reported by the author, and he claims avoidance of certain dangers inherent in other instruments. He gives a well-considered section on the use of the curette, with careful enumeration of its possibilities for harm, and while here, as elsewhere throughout the book, the judicial, or rather non-partisan attitude, is maintained, it is plain that his opinion is adverse to the curette, in acute cases at least. This is in accord with the view of most competent men of the present day. It is somewhat surprising that the valuable curettement forceps of Emmet is not mentioned, since this instrument is free from the objections rightly urged against the curette, and, theoretically at least, seems preferable to the *écouvillon*.

Readers of this chapter will note with interest that in the treatment of localized pelvic inflammation without suppuration, the Bier method is advocated. The general treatment of infected patients receives adequate attention, and it is interesting to note the unfavorable criticism of alcohol. What a shock the present-day attitude regarding this drug would be to the active men of a generation ago!

A full consideration of the various means to produce leukocytosis, as nuclein, saline solution, and colargol, is given, but, of course, no definite statements are permissible as to their specific value. After a very clear and concise enunciation concerning the much vaunted antistreptococcic sera, the conclusion is reached that their value is at best questionable. The hope is, however, expressed that there will be developments along this line, with better results in the future.

In the chapters upon the operative treatment there is nothing new, but the conservatism is praiseworthy, and we are particularly glad to note this quality in the advice given regarding acute pus tubes and ovarian abscess, and also in the narrow indications admitted for hysterectomy. We can not close this review without again expressing our admiration for the work. It is by far the best book upon this subject as yet published, and should have a wide circulation.

W. R. N.

PRACTICAL PATHOLOGY. By ALDRED SCOTT WARTHIN, Ph.D., M.D., Professor of Pathology and Director of the Pathological Laboratories in the University of Michigan. Second edition; pp. 321; 55 illustrations. Ann Arbor: George Wahr, 1911.

THIS is a manual of autopsy technique written primarily for students, but valuable to anyone engaged in such work. Part I, comprising 198 pages, is a very thorough consideration of the autopsy proper. Part II, comprising 111 pages, describes the laboratory treatment and examination of material obtained at autopsy. The preliminary portion of Part I, containing the legal restrictions relating to autopsies, the order of autopsy and a list of structures that should be examined, suggestions as to protocols, and the external examination and the signs of death, is unusually complete. The description of removal and examination of the organs is clear and thorough. For the removal of the spinal cord both posterior and anterior methods are described, and for opening the heart four methods are given. After the removal of each viscus, the pathological changes especially to be looked for in the organ are noted. A chapter is devoted to the autopsy of the newborn and another to the medicolegal autopsy, with a description of the characteristic lesions due to twenty-five common poisons.

In Part II the use of the freezing microtome and all of the common methods for fixing tissues are described, with the especial advantages and disadvantages of each. At least one staining method, and, as a rule, several, is given for each kind of tissue, and for each kind of degeneration, infiltration, and exudation; no attempt is made, however, to give all the modifications of a staining method. Bacteriological methods are not considered except the staining of microorganisms in tissues and in smears, with the staining reaction of about forty common bacteria, yeasts, and animal parasites.

About half the illustrations are of autopsy instruments and common laboratory apparatus; however, the remaining ones are well selected to illustrate methods of exposing, or examining, various organs. The material in the book is clearly presented, well arranged, and adequately indexed.

J. H. A.

REVUE DE MÉDECINE MÉMOIRES RÉDIGÉS EN L'HONNEUR DU PROFESSEUR RAPHAËL LEPINE A L'OCCASION DE SA RETRAITE PAR SES ELÈVES ET SES AMIS. Pp. 885; 20 illustrations. Paris: Félex Alcan, 1911.

OPPOSITE a full-page portrait of Professor Lepine is found this dedication with which the book opens: "To the Master who being a scientist wished to be always a physician, to him who

has been the respectful servant of observation, but who has taken Pathological research as a foundation for all and who has taken as a starting point for all medical action Physiology, Pathological Anatomy, Biological Chemistry and Experimentation, to him who has taken a great part in the revival of Medicine and who still preserves it in his studious retirement, to the educator who has said, 'The physician should think physiologically,' to Professor Raphaël Lepine."

It is in these words that his pupils, associates, and admirers dedicate this volume in honor of Professor Lepine on the occasion of his retirement after over thirty years' continuous service as a member of the Medical Faculty of Lyons. It was about 1875 that Lepine, who as one of Charcot's brilliant pupils was well fitted for the position, was called to a chair of the Medical Clinic at Lyons, directly concerned with the introduction of scientific investigation and laboratory methods. His success was remarkable, as a glance at the breadth of scope and progressiveness of his bibliography would suggest.

The collection of papers gathered in this volume consists of one hundred and twelve contributions, the majority by members of the Faculty of Lyons, but including also prominent writers from other parts of France, Italy, and England. The subjects are as various as the interests of the many authors, and no attempt has been made to confine the articles in any way so that many concern the specialities. As a whole, the volume commands respect as must any group of papers which contain in the list of its authors such names as Achard, Lauder Brunton, Favre, Patella, Roger, and Weill.

To attempt to select individual articles for commendation from such a number is difficult and reflects merely the reviewer's personal interests. Such is the contribution of Maurice Letulle, Professor to the Faculty of Medicine of Paris, on Cysts of the Kidney. In this 25-page monograph is a clear detailed description of the various types of cyst found in healthy and pathological kidneys with illustrations of microscopic sections through them. The great number of the articles and the great diversity of subjects, if nothing else, make this book of great interest, for although no epoch-making contribution is contained and but little original work reported, yet we may here make the acquaintance of a group of the French medical teachers and writers and obtain a sort of bird's-eye view of French medical thought.

The volume is very creditable and a fitting tribute to a man who not in his own country alone, but throughout the entire scientific world is held in high esteem and honor.

O. H. P. P.

THE ORIGIN OF LIFE. By H. CHARLTON BASTIAN, M.D., F.R.C.S.,
Emeritus Professor of the Principles and Practice of Medicine.
Pp. 119; 10 plates. London: University College, 1911.

THE author presents in this book some researches which the British Royal Society found unsuitable for acceptance. He has demonstrated the appearance of a few *torulæ*, bacteria, and moulds in hermetically sealed tubes, containing a solution of sodium silicate with either ammonium phosphate and phosphoric acid, or liquor fevri nitratis, in from four weeks to twelve months after the sealed tubes have been heated in a bath of from 100° to 130° C. for ten to twenty minutes. He has further shown that these organisms so obtained are alive, by transplation into sterile bouillon with immediate abundant growth of the organisms in this medium. A careful reading of the book, however, fails to show that the author has determined the temperature attained within the sealed tubes during the so-called sterilization, nor does he report any control experiments to rule out the possibility of having merely lowcred, without extinguishing, the vitality of organisms originally present in the tubes. The work in consequence would seem to be, until further controlled, of but little value for the drawing of any definite conclusions and certainly does not warrant the author's assumption that his findings are an evidence of spontaneous generation. The title of the book is, therefore, misleading. The plates are photomicrographs of some of the organisms found in the tubes.

J. H. A.

MINOR SURGERY. By L. A. BIDWELL, F.R.C.S., Surgeon of the West London Hospital; Dean of the Post-graduate College; Consulting Surgeon to the Blackheath and the Charlton Hospitals. Pp. 205; 88 illustrations. London: Hodder and Stoughton and Frowde, 1911.

THE work being a manual aims to give simple, clear, practical directions for the performance of every-day minor surgical work. No attempt has been made to give the several methods that may be useful in accomplishing the desired result, but rather the author has given that which he, in his experience, has found to be the best.

Emergency operations of the minor and a few of the major type are described in practical detail. In many instances the author has given interesting facts not generally known or appreciated.

The work is a valuable one for hospital internes, students, and the busy general practitioner, as it contains many facts that can be obtained only through association with some one doing a large amount of this work. Furthermore, it describes many of the

minor practices which the larger works deem too elementary for consideration.

The book is well written and the style is pleasant. The facts are condensed and there is no useless reading of theories, possibilities, or diverse opinions.

E. L. E.

AN INTRODUCTION TO SURGERY. By RUTHERFORD MORISON, M.A., M.B., F.R.C.S., Professor of Surgery, University of Durham. Pp. 162; 146 illustrations in the text and 5 colored plates. New York: William Wood & Co., 1911.

THIS book is an abstract of the author's lectures on surgery and is an interesting summary of the modern point of view of the subject discussed. It includes inflammation, ulcers, gangrene, syphilis, tubercle, malignant disease, hemophilia, wounds, certain disturbances of the abdominal and pelvic viscera, and certain indications for operation. The general scheme or outline of the book is most unsatisfactory, but the subject matter contained therein is important and discussed in a most interesting manner. The work should be exceedingly valuable to those who are students of Mr. Morison and contains a number of chapters of which use may be made with advantage by teachers of surgery, but to the general practitioner or to the student at large it is apt to prove unsatisfactory, owing to the incompleteness of the subject discussed and to the failure to include many important things. The illustrations are excellent and the general make-up of the book very satisfactory.

G. P. M.

THE MECHANISM OF LIFE. By Dr. STÉPHANE LEDUC, Professor a l'école de Médecine de Nantes. Translated by W. DEANE BUTCHER, Formerly President of the Röntgen Society, and of the Electro-therapeutical section of the Royal Society of Medicine. Pp. 172; 63 illustrations. New York: Rebman Company, 1911.

THIS interesting book gives a clear presentation of some of the more important physical and physicochemical laws that must be taken into account in considering organic life and its phenomena, including the laws of colloids. It also presents some relatively new observations on diffusion and on osmotic growths that may become an aid in the interpretation of phases of cellular activity. These osmotic growths are inorganic products produced under certain experimental conditions which, in structure and activities, show an extraordinary analogy to simpler forms of organic life.

Some kinds have been produced by many observers, and the author gives directions for repeating such experiments as are original with him. At times the author draws from his observations conclusions which his readers will probably not accept. This is especially true of his speculations upon the nature of light, upon spontaneous generation, and upon the cause of the rhythmic character of the heart beat. He is also too ready to explain by simple physicochemical laws alone, some of the most complex of cellular activities. One cannot read the chapter on karyokinesis, however, without feeling that the observations presented must be of great significance in explaining this phenomenon. The illustrations are photographs of the forms obtained in diffusion experiments and of osmotic growths and are most interesting.

As the result of collaboration between the author and the translator this English edition has some advantage over the original French edition.

The book will well repay a careful reading.

J. H. A.

THE PROBLEM OF RACE BETTERMENT. By J. EWING MEARS, M.D., LL.D. Pp. 45. Philadelphia: Wm. J. Dornan.

WITHIN this title are included three papers, published in various medical journals, and the subject matter contains only about 40 pages. The subject, however, is extremely well handled and forcibly written. It is needless to say that everyone will agree with the author that something should be done to diminish the ever-increasing number of idiots, imbeciles, criminals, and epileptics who are constantly born into what seems to be a lawless sphere, at least in so far as this particular subject is concerned. However, since the publication of the first of these papers, laws have been enacted in some of the States to desexualize this class of patients, notably in the State of Indiana. Because of the very nature of our Republic in so far as matters of health are concerned, we are woefully back of the more central types of government, such as Germany, which readily control social questions. It is simply another argument for the establishment of a national Bureau of Health and of a Secretary of Health in the Cabinet of the President.

T. H. W.

LES SYNCINESIES. By LE DOCTEUR G. STROEHLIN, Ancien Interne des Hôpitaux de Paris. Pp. 147. Paris: G. Steinheil, 1911.

THIS is a thesis upon the general subject of associated movements. No new conclusions are presented.

T. H. W.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Effects of Subdural Injections of Leukocytes on the Development and Course of Experimental Tuberculous Meningitis.—MANWARING (*Jour. Exper. Med.*, 1912, xv, 1) finds that, though the mechanism of cure for tuberculosis has not been fully worked out, it would appear that the phagocytic cells play an important part, since it has been shown that leukocytes injected simultaneously with tubercle bacilli have the power of decreasing the pathogenic properties of these organisms. Manwaring has conducted experiments on dogs to study the effects of injected leukocytes on the development and course of experimental tuberculous meningitis. The cerebrospinal membranes are almost impervious to the blood proteids, and so normally receive little or no protective substance from this source, and few, if any, leukocytes. Hence the meningeal cavity is always in an inferior condition of defence against infection. His observations consisted in trephining dogs, and after healing, injecting them intradurally with strains of varying virulence of bovine and human tuberculosis. At the same time in certain animals, sterile leukocytes, obtained by the intrapleural injection of turpentine, were injected. By the injection of tubercle bacilli in this way, a disease is produced after five to thirty days' incubation, characterized by increasing paralysis, and terminating almost invariably in death. The pathological picture varies with the virulence and dosage of the organisms. It shows meningeal thickening with adhesions. The subdural space usually has an active tuberculous process varying from an accumulation of fluid, fibrin, and semi-necrotic cells, to well-organized masses of diffuse tuberculous tissue. Tubercle bacilli are present. Manwaring found that if leukocytes were

injected with organisms, though one-quarter of the animals died within a few hours—many with no accessory cause found—in those that lived there occurred uniformly a marked delay in the development of a paralysis, and a marked prolongation of life depending on the virulence of the organism used.

Intramuscular Injections of Defibrinated Blood in Anemia.—P. ESCH (*Deut. med. Woch.*, 1911, xxxvii, 1943) reports the use of intramuscular injections of defibrinated blood in the treatment of anemia. Human blood is employed, and the injections are made into the gluteal region. As much as 30 c.c. are given at a time. It is important, Esch says, to determine that the end of the needle is not in a vein, so that intravenous injection may be avoided. Favorable results are reported in a case of pernicious anemia following pregnancy and in secondary anemias.

The Incoagulable Nitrogen of the Blood in Nephritis and Uremia.—H. HOHLWEG (*Deut. Arch. f. klin. Med.*, 1911, civ, 216) has studied the incoagulable nitrogen (*Reststickstoff*) of the blood serum in nephritis, using the method devised by himself and H. Meyer. His results confirm those of Strauss and several other workers. The blood was always obtained between 10 and 11 A.M., the patient receiving only a cup of milk and a roll for breakfast, so that the effect of digestion might be fairly constant. About 150 c.c. of blood were withdrawn from an arm vein and placed in the ice-chest to allow the serum to separate. The serum was then used for the determinations. It was found that the normal average incoagulable nitrogen is 0.051 gram per cent., the extremes being 0.041 gram and 0.060 gram. The results of the study summarized as follows: (1) The incoagulable nitrogen of the blood serum of patients without renal diseases averages 0.051 gram per 100 c.c. serum; of this 11.7 per cent. is precipitable by tannin; 27.4 per cent. is not precipitable by tannin; 60.8 per cent. is urea. (2) In nephritis the incoagulable nitrogen rises to 0.63 to 0.93 gram per cent. Essential differences in the values in parenchymatous and interstitial nephritides are not discoverable, either in the total incoagulable nitrogen or in its fractions. (3) The values found in nephritis exhibit no noteworthy increase when uremia develops, so long as the patient's condition is susceptible of improvement. Thus, total incoagulable nitrogen of 0.060 to 0.095 gram per 100 c.c. makes the prognosis relatively good, provided other complications, such as cardiac disease do not appear. (4) In the last weeks or months of life of a nephritic, the incoagulable nitrogen of the serum increases rapidly or slowly to the highest values known, whether or not uremic symptoms exist. The increase is progressive to the time of exitus. (5) These enormous collections of incoagulable nitrogen—up to 0.370 gram per cent.—are due almost wholly to increase of the urea fraction, which may amount to 80 per cent. of the total incoagulable nitrogen. There is a slight increase in the fraction which is not precipitable by tannin. No change is observed in the tannin-precipitable fraction. (6) The increase of the incoagulable nitrogen is merely the expression of renal insufficiency, and is in no way specific for uremia. (7) In nephritics who die of other diseases, as affections of the heart, no such striking accumula-

tion of the incoagulable nitrogen is seen in the serum. In patients without renal disease, normal values are found, even in the last hours of life. Increase of the incoagulable nitrogen above 0.120 grams per cent. is characteristic of nephritis which will soon terminate fatally. (8) In cases of doubtful diagnosis, the quantity of the incoagulable nitrogen may be of aid. In prognosis, too, valuable information may be gained.

The Relation of Bovine Tubercle Bacilli to Human Infections.—H. KOSSEL (*Deut. med. Woch.*, 1911, xxxviii, 1972) contributes a study of the relative frequency of infection of man with human and bovine tubercle bacilli. Of 709 patients with pulmonary tuberculosis, two cases were definitely bovine alone, and probably a third, in one case both human and bovine bacilli were demonstrated, while in 705 instances the human type of bacilli alone could be found. Such findings as these indicate beyond question the correctness of Koch's views that human tuberculosis owes its widespread prevalence to direct transmission from man to man. The elimination of the bovine source would cause a scarcely appreciable reduction in the incidence of the disease.

Acetonuria in Diphtheria and Acute Anginas.—F. REICHE (*Münch. med. Woch.*, 1911, lviii, 2153) has contributed valuable statistics on the occurrence of acetonuria in diphtheria and acute anginas. In all, the urine from 3826 patients has been studied. Of these, 3200 were acute diphtheria with Löffler's bacilli in the exudate. Acetonuria was demonstrable with the sodium nitroprusside test applied directly to the urine in 2079, or 65 per cent. of the cases. The duration of the acetonuria was usually only a few days, at times one day; less often it persisted a week or more. The great majority of all cases of acetonuria occurred between the first and fourth days of the disease. Since many patients entered the hospital late in the disease, it is quite possible acetonuria had existed earlier, but had disappeared before urinary examinations were begun. Most of the cases were found in patients under fifteen years of age. The height of the temperature has little effect, but acetone is much commoner in the severe forms of the disease. Diet seemed to play a small part in the production of acetonuria, since many of the patients exhibiting it were receiving carbohydrates. Among 390 cases of follicular angina, 159, or 40.8 per cent., showed acetone in the urine. In 172 cases of angina simplex, acetonuria occurred in 44, or 25.6 per cent. Sixty-four cases of quinsy were studied. In 25 the abscess had been incised or had ruptured previous to admission. In all of the remaining 39, acetonuria was present.

The Technique of Hemoglobin Determinations.—C. STAUBLI (*Münch. med. Woch.*, 1911, lviii, 2429) has noticed, in using the Autenrieth and Königsberger colorimeter for hemoglobin determination, that the results vary according to the time interval between diluting the blood with tenth-normal HCl and making the reading. As the blood-HCl mixture stands, its color darkens. This observation led to a thorough investigation of the phenomenon. In using the Autenrieth and Königsberger colorimeter, 20 c.mm. of blood are mixed with 2 c.c. of tenth-normal HCl. After preparing this mixture, Stäubli made colori-

metric determinations at the end of one-half, two and one-half, five, ten, fifteen, twenty, twenty-five, and thirty minutes. He found that the mixture becomes progressively darker. The darkening of the fluid is more rapid in the earlier minutes. By plotting the values found, the curve obtained is a parabola, and from a study of this Stäubli recommends that the reading be made at the end of ten minutes. After this time has elapsed the darkening of the solution is slight and the error small. Greater relative increases are observed when the hemoglobin is low than with high values. In using the Sahli hemometer, 20 c.mm. of blood are diluted with 0.2 c.c. of tenth-normal HCl (*i. e.*, 10 divisions of the graduated tube), and after one minute the contents are diluted with water till the color is like that in the standard tube. Here the strength of the HCl is so greatly diminished by dilution with water that darkening of the solution is much less pronounced than with the Autenrieth-Königsberger colorimeter. It is essential, however, that Sahli's directions be rigidly adhered to. (1) Tenth-normal HCl is filled into the graduated tube exactly to the mark 10. A greater amount of acid will accelerate the darkening. (2) The acid should be tenth-normal. (3) Wait exactly one minute after adding the blood, and then dilute with water. The dilution with water inhibits the darkening effect of the acid. (4) Stäubli would add a fourth direction, *i. e.*, to make a maximal dilution with water as quickly as possible. He suggests that a still better procedure for determining hemoglobin with Sahli's hemometer is the following: The blood-HCl mixture is diluted at once with tenth-normal HCl till the color is approximately that of the standard tube; then wait ten minutes to make the final colorimetric determination. This final dilution, which will require only a few drops, may be made either with water or acid. With this technique the results are uniform. Whatever method is followed, it is absolutely essential that it be adhered to strictly, in order that the results may be comparable.

The Influence of Some Foodstuffs on Gastric Secretion.—F. CRAVEN MOORE and H. E. ALLANSON (*Proc. Roy. Soc. Med.*, London, 1911, Medical section, 19). The observations of Pawlow and his co-workers having established the varying influence of different diebetic substances on the rate of gastric secretion, and the activity of the secreted juice in the dog, it was accepted as at least highly probable that a similar relation would obtain in the human, and in a limited fashion the truth of this has already been established. It seemed of some practical importance to determine by observation in humans, the effect on gastric secretion of certain foodstuffs which have been credited empirically with having some particular relation (ameliorative or causal) with certain disorders of the stomach. Fifteen individuals, including normal subjects and those with and without definite gastric disorder were used. A test breakfast of 4 breakfast biscuits, 10 ounces of tea, coffee, cocoa, without milk or sugar; milk, albumin water containing the white of one egg in 10 ounces of water, 2 teaspoonfuls of meat extract in 10 ounces of water, or 2 ounces of whisky in 8 ounces of water were given on a fasting stomach. The contents were removed an hour later, and tested for free HCl and total acidity. On the average, not less than three experiments were made with the particular substance under

consideration. For control, a test breakfast of 4 biscuits and 10 ounces of water was used. Moore and Allanson in this way found that tea induces more secretion than water, but with varying personal relation; that coffee is more powerful than tea, but with individual susceptibility more marked; that cocoa is more stimulating than water, but less than tea; milk is less than water, probably depending on the inhibitory action of its fat; meat extract is very powerful, while albumen water seems to exert a considerable stimulating effect on gastric secretion. The effect of alcohol and tobacco was tried on two normal individuals, showing that either agent may have a stimulating or a depressing effect on secretion, probably in accordance with the personal susceptibility.

Serodiagnosis of Malignant Neoplasms.—P. v. MONAKOW (*Münch. med. Woch.*, 1911, lviii, 2207) has investigated the serodiagnostic test for malignant tumors which was described independently by Freund and Kaminer and by Neuberg. These authors observed that the blood from a carcinomatous patient does not digest cancer cells, whereas normal sera dissolve them. The reaction may fail with normal sera and occasionally cancerous sera cause solution of cancer cells. V. Monakow has examined sera from 15 patients with cancer and 52 sera from non-cancerous individuals. His results are in accord with those of other observers. Combining the statistics reported in literature with his own, he finds that 77 per cent. of normal sera dissolve cancer cells, while 23 per cent. have no effect. Of carcinomatous sera 21 per cent. digested cancer cells, the remaining 79 per cent. producing no solution. The reaction is, therefore, not specific, and must be interpreted with extreme caution.

Fungus Tracheobronchitis.—GEORGE HOWARD HOXIE and FREDERICK C. LAMAR (*Jour. Amer. Med. Assoc.*, 1912, lviii, 95) report 2 cases of bronchitis in which careful examination of the sputum revealed the presence of fungus stalks as the only causative agent. In the first case the symptoms were those of tracheobronchitis with spasmodic cough, relieved by the discharge of pin-head nodules. Such contained stalks of a fungous type, and many bodies the size of epithelial cells. Scrapings from mouth did not show them. The second case was characterized by cough for one year, with one hemorrhage. There were no signs of tuberculosis. The sputum was negative save that it contained an unidentified fungus, growing on potatoes. Hoxie and Lamar believe that the source of infection may have been food, as both patients were vegetarians. They find the literature on the subject very scanty. In America there are no case reports save on streptothrix. They believe the condition is more frequent than the lack of literature indicates, and report these cases with the hope of similar reports, and possible identification of the responsible fungi.

Characteristic Reactions Appearing in the Urine after the Administration of Atophan.—W. SKORCZEWSKI and I. SOHN (*Wien. klin. Woch.*, 1911, xxiv, 1700) have noted several reactions, hitherto undescribed, which appear in the urine after administration of atophan. Skorczewski and Sohn find (1) that the addition of a few drops of the urine to concentrated hydrochloric acid colors the latter canary yellow.

(2) Treated with phosphotungstic acid, the urine of patients receiving atophan yields a yellow precipitate, whereas with normal urine the precipitate is reddish gray. (3) Addition of ammonium sulphate solution and ammonium hydrate colors the urine dark green. Normal urine retains its yellow color. (4) The urine gives the characteristic Ehrlich's diazo reaction. The first three reactions appear within two hours after giving the drug, and are lost one to two days after discontinuing it. The diazo reaction appears twenty-four hours after administration of three grams daily. Skorezewski and Sohn have shown that these reactions are directly attributable to the drug. They have also demonstrated that atophan-urine is capable of reducing potassium permanganate to a certain extent, so that the Folin-Shaffer method for determining uric acid quantitatively is inapplicable in such urines.

The Diagnosis of Renal Lues.—R. BAUER (*Wien. klin. Woch.*, 1911, xxiv, 1458) has made observations on several cases of renal syphilis which he sums up in the following sentences. Luetic infection is undoubtedly capable of causing renal disease, but this is nevertheless rare. The disease may be due to toxins or to a direct invasion of the kidneys by the spirochetes. Unexplained amyloid disease of the kidney is always strongly suggestive of lues. A positive Wassermann serum reaction is, of course, of great value in the diagnosis, and is usually well marked with renal lues. A positive Wassermann reaction in the urine appears to be equally constant. With abundant globulin in the urine (8 to 10 per cent. of the total protein), the reaction is positive in the native specimen, otherwise only in the globulin fraction. At the present time, however, a positive urinary Wassermann reaction has no more significance, so far as the condition of the kidneys is concerned, than a serum reaction.

The Effect of Hydrogen upon the Alimentary Enzymes.—Since hydrogen peroxide has been recommended in the treatment of hyperacidity of the stomach, the observations of L. E. WALBUM (*Berl. klin. Woch.*, 1911, xlviii, 1929) of its action on the alimentary enzymes are of interest. He finds that ptyalin is markedly affected by hydrogen peroxide. A 0.02 per cent. solution inhibits its action slightly, while 0.1 per cent. and stronger solutions practically destroy ptyalin completely. Pepsin and trypsin are relatively immune to its action. They are not destroyed by 0.5 per cent. solutions. Rennin, on the other hand, is very sensitive to hydrogen peroxide, being completely destroyed by a 0.5 per cent. solution and measurably inhibited by a dilution of 1 to 3000.

A Röntgenologic Study of Spastic Obstipation.—G. SINGER and G. HOLZKNECHT (*Münch. med. Woch.*, 1911, lviii, 2537) report a Röntgenologic study of spastic constipation. In the great majority of the cases a marked degree of hypertonicity was found in the distal portion of the colon. Contrasted with this, the proximal portion of the large bowel exhibits normal tonicity with hypermotility. The line of separation between these two portions is variable in location, but is always found somewhere between the hepatic flexure and the end of the descending colon.

SURGERY

UNDER THE CHARGE OF

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Phosphaturia and Oxaluria.—TEISSER (*Ann. d. mal. d. org. gén. urin.*, 1911, ii, 2113) says that the liver appears to be the organ regulating the deposits of phosphorus and the essential instrument of the dehydrating process, bringing about the different transformations which under the influence of the synthetizing organs (liver and brain) cause the changes in the mineral phosphates introduced in food, into those various combinations (glycophosphoric acid, lecethins, neucleins, etc.) in which forms the phosphorus becomes fixed in the living cells. But when the function of the liver is disturbed (even by a transitory inhibition) this regulation will be interfered with. Either the hydrolytic or the anhydrant process will be disturbed and the phosphorus will remain in the condition of mineral phosphates, therefore, no longer being directly useful. The excess will be eliminated by the urine or feces. The more pronounced transitory or chronic phosphaturias have always appeared to coincide with grave affections of the hepatic gland, principally cirrhosis of the liver. This is well supported by the statistics. In recent years Teisser has encountered several times chronic phosphaturia in the diabetic form, coinciding with acetoneuria or only with acetone vomiting.

RICHTER (*Ann. d. mal. d. org. gén. urin.*, 1911, ii, 2144) says that these condition are caused in all cases by a change in the proportion of the soluble and insoluble phosphates in the urine. There is no increase in the phosphoric acid. The phosphaturia may be: (1) Exogenous or alimentary, the food being too rich in alkaline substances (alkaline urine). (2) Gastrogenous from the excessive production of pepsin in the digestive tract, and of some irregularity in its absorption. This form of phosphaturia may be physiological or pathological. (3) Endogenous from some disturbance in the assimilation of calcium, an excessive quantity of this substance showing itself in the urine instead of being eliminated by the rectum. This method of expelling the lime is not due to any affection of the excretory organs (kidneys or rectum), but rather to some disturbance of metabolism. It is a disturbance of what may be called the internal secretion, the precise nature of which we do not know. An etiological treatment, which consists in regulating the elimination of the excess of calcium, is possible only in this latter form. In all the other forms, especially those which are called nervous,

and in those for which the urogenital system and rectum are responsible, the treatment should be limited principally to the nervous system.

HOGGE (*Ann. d. mal. d. org. g n. urin.*, 1911, ii, 2145) says that in most cases the phosphaturia is probably due to a secretory neurosis of the kidneys; at least one can say that the phenomena appear to be due to an influence upon the renal nervous system, which modifies the reaction of the urine. Aside from the diabetic phosphaturia of Teisser and the juvenile phosphaturias of the German writers, phosphaturia ought to be considered as a benign symptom from the point of view of the internist. In general one can say that phosphaturia is to be compared with azoturia, and that it is found in acute consumptives. In the chronic consumptive conditions, on the contrary, the organic combustion is more economical, and there is at the same time as hypoazoturia, a diminution in the elimination of the phosphates. From the surgical point of view, phosphaturia aggravates and complicates inflammatory diseases and lithiasis of the urinary apparatus. The best symptomatic treatment of phosphaturia consists in the administration of abundant liquids, of urotropin, in the choice of foods and in rules for hygiene and diet. Permanent phosphaturia indicates always an important disturbance in the general nutrition.

Alcohol Injection of the Gasserian Ganglion for Trigeminal Neuralgia.—HARRIS (*Lancet*, January 27, 1912, 218) says that during the last three and one-half years he has seen 90 cases of intractable trigeminal neuralgia, 86 of whom he has treated with alcohol injections. In only 3 cases was no relief obtained owing to the nerve not being found. In 3 others slight definite improvement resulted, and in the remaining 80 cases complete relief was obtained for intervals varying from as little as two months and four months in 2 cases, to two and one-half years and more. For the majority, twelve months of complete relief from pain may be looked for as a minimum, if the nerve is definitely hit and anesthesia produced; while two to three years and more may be expected when the depth of anesthesia indicates that the nerve has been properly destroyed. Strong alcohol injected into any nerve trunk destroys the nerve fibers almost immediately, and total loss of function will occur until regeneration takes place. The extirpation of the ganglion gives a permanent cure, but its severity deters a large number of sufferers from seeking relief by this means. Harris has tried to improve on the technique of the deep injection of alcohol by carrying the alcohol through the foramen ovale into the Gasserian ganglion itself, in order that by destroying the nerve cells in the ganglion regeneration of nerve fibers along degenerated trunks shall be prevented, and a permanent cure be thus obtained. During the last fifteen months he has injected the ganglion through the foramen ovale with 90 per cent. alcohol in 7 cases. The first was done thirteen months ago, and he still remains perfectly well, with no pain of any kind. Harris' technique for injecting the Gasserian ganglion varies only in detail from that of injecting the inferior maxillary nerve at the foramen ovale; instead of inserting the needle close below the lower border of the zygoma, he chooses a point either on or slightly below the line joining the incisive notch to the ala nasi. This line in the average skull, when the teeth are in position, corresponds to the lower

border of the sigmoid notch of the lower jaw. To reach the foramen ovale, therefore, the needle must be directed slightly more upward, making it thus easier to pass the point through the foramen. As soon as the nerve is reached at the foramen, he injects it with 90 per cent. alcohol, using about 1.5 c.c., but if no general anesthesia is being given, he precedes the injection of alcohol by injecting 6 or 7 minims of 2 per cent. eucaine solution into the nerve, thus rendering the subsequent injection of the alcohol comparatively painless. If these results, immediately, deep anesthesia of the lower lip and chin from injecting the nerve itself, he then feels for the lip of the foramen ovale with the point of the needle, if this has not already been felt. Sometimes the needle slips easily through the foramen, sometimes it has to be worked through, but no degree of force should be used. Sometimes after pushing the needle through the foramen ovale, the point of the needle may leave the nerve tissue and enter the cave of Meckel, and cerebrospinal fluid may drip from the needle. If the injection of alcohol be then commenced no resistance will be felt to the push of the piston, and instantly the patient will complain of severe headache at the base of the skull and back of the head. Should this occur the needle must be partially withdrawn, and then worked through at the posterior edge of the foramen, so as to keep the point within the substance of the ganglion. Injection for the second division at the foramen rotundum is usually more difficult than for the third division at the foramen ovale, and in a certain proportion of cases it is impossible. There is also more likelihood of hematoma from wounding the internal maxillary vessels. These points are additional reasons for preferring the injection of the Gasserian ganglion through the foramen ovale.

The First and Last Kink in Chronic Intestinal Stasis.—LANE (*Lancet*, December 2, 1911, 1540) calls particular attention to the last kink or obstruction in our drainage scheme which affects the large bowel where it crosses the brim of the pelvis on the left side. It is so arranged as to oppose the backward passage of feces from the pelvic colon into the large bowel, which is likely to take place if the kink or obstruction is not efficiently developed. When Lane first performed ileocolostomy for chronic intestinal stasis, he divided the ileum and put it into the sigmoid loop. At the same time he took great precautions to free the obstruction at the pelvic brim referred to. This operation was frequently followed by backward passage of material along the descending, transverse, and ascending colon to the cecum, often necessitating the removal of the large bowel at a later date. This led to the removal of the large bowel down to a level of the junction of the ileum with the sigmoid, performing both operations at the same time. In order to avoid the removal of the colon and to reduce materially the risk of the operation, he effected a communication between the ileum and the large bowel in the true pelvis below the level of the last kink. This he found most successful. He believes that no one can become affected by tuberculous disease or by rheumatoid arthritis unless the resisting power of the individual to the entry of organisms has been depreciated by auto-intoxication consequent on the presence of chronic intestinal stasis. So in these conditions and especially in the case of progressive tuberculous affections of joints,

Lane employs no local operative procedures to the affected joint other than rest, and if necessary, aspiration of any fluid material that does not readily become absorbed after the operation; but proceeds to free the patient of the auto-intoxication by putting the ileum into the pelvic colon below the kink at the brim of the pelvis. In these cases the results of operation have been most successful, and the patient has improved both locally and generally. An obstruction develops frequently in the end of the ileum which plays an important part in the production of the group of symptoms which are regarded by the physician as evidence of indigestion. This plays an important part in the development of disturbances in the duodenum and stomach.

Infection of the Iliopsoas Muscle from Appendicitis.—MAUCLAIRE and AMAUDRUT (*Arch. gén. d. Chir.*, 1912, vi, 33) say that infection of the iliopsoas muscle, suppurative or non-suppurative, is a rare complication of appendicitis. Clerget collected 83 cases in which this muscle was infected. Of these, 13 were on the left side and 70 on the right side. Of those on the left side, one was caused by a perisigmoiditis, one by a salpingitis, one by an osteomyelitis of the pelvis, and one by a suppurative arthritis of the sacro-iliac joint. Of those on the right side, only 35 could be ascribed definitely to an appendicitis, while one or two more were doubtful. The others were due to direct trauma, puerperal infection, typhoid fever, or influenza. Mauclore and Amaudrut report a case in which the infection of the muscle followed a mild appendicitis. Perforation of the appendix occurred in the second attack with a resulting infection of the muscle but not of the peritoneal cavity. Death followed operation, and although an autopsy was performed, the cause of death was not ascertained. It is concluded that while the condition is very rare it is grave. This complication seems to have some relation to an abnormal anatomical condition of the appendix, which after traversing an abnormal diverticulum situated under the iliac fascia, by its extraperitoneal extremity comes into direct contact with the psoas muscle. In the great majority of cases the appendix is in a retrocecal position. In 27 per cent. of the cases there had been one or more preceding attacks of appendicitis. The infection of the muscle can develop under two forms: One mild without suppuration, one grave with suppuration, which is more frequent than the other. In this form the local symptoms indicate the formation of an abscess, apparently tardy, toward the tenth or fourteenth day of the disease. The inflammation of the muscle is always accompanied by a grave general condition. Death occurred in 27 per cent. of the cases, notwithstanding operation, which should be done as early as possible.

Motor Insufficiency Due to Perigastritis of Gonorrheal Origin.—GREKOW (*Zentralbl. f. Chir.*, 1911, xxxix, 105) says that little attention has been paid to perigastritis, especially that which leads to impermeability of the pylorus and consecutive motor insufficiency of the stomach. The most frequent causes are associated with affections of the stomach and duodenum, as from ulcers and other affections. It may result from a focus in a distant organ as from perityphlitis, or diffuse peritonitis of various origins. Grekow believes that it can

result from tubal disease and that the gonococcus is particularly prone to produce it. He reports the case of a girl, aged eighteen years, who was admitted for a gonorrhea which was associated with a pelvic peritonitis. She was discharged July 20, 1909, with all symptoms improved except the occasional vomiting. She returned, however, two days later, with exacerbation of pain in the region of the stomach, and vomiting so frequent that the taking of food was impossible, and she was pale and thin. Her health previous to the beginning of the present trouble had always been good. No lues. No blood in the vomit or feces. Vomiting two or three times daily. Stomach dilated and palpable. Repeated tests showed no hydrochloride in the stomach contents. No tumor palpable. Operation, August 8, 1909, under local anesthesia. Stomach markedly dilated and lowered, and its walls hypertrophied. Numerous moderately loose adhesions in the region of the pylorus and gall-bladder. The omentum was loosely adherent to the right uterine adnexa, and contained enlarged and soft glands. In the remaining portions of the peritoneal cavity were found radiating adhesions. The pylorus had the appearance of a ring formed somewhat like a solid tumor. Neither the pylorus nor the duodenum showed any signs of a recent ulcer. No adhesions of the hepatic flexure of the colon, and the gall-bladder was free of stones or other changes except that its serous surfaces were rough and covered with a fine membrane. Appendix small and movable and unchanged. The adhesions were for the most part bluntly broken up. A posterior gastro-enterostomy with a Murphy button was performed, besides a gastroplication and gastropexy. The patient quickly improved and left the hospital well three weeks later. Three months after the operation she had a florid appearance, was free of symptoms, and had increased in weight 23.8 kilograms. This is a typical example of hypertrophy of the pylorus with dilatation of the stomach. The cause was the adhesions in the region of the pylorus which were undoubtedly due to the gonorrheal peritonitis. In a second case there was a diffuse peritonitis with dilatation of the stomach from rotation of the pylorus and duodenum as well as a slight hypertrophy of the pylorus.

The Formation of a New Bladder and a New Urethra.—HEITZ-BOYER and HOVELACQUE (*Jour. d'Urolog. Med. et Chir.*, 1912, i, 237) say that the urine from the kidneys accumulate in a continent reservoir (the bladder), provided with an excretory canal (the urethra). These are accessible to instrumentation from without and every operation to correct a deficient reservoir should meet these requirements, whether the defect is the result of a congenital malformation (extrophy of the bladder), or of an accidental cause (total cystectomy, grave vesicovaginal fistula, etc.). Heitz-Boyer and Hovelacque conceived such an operation, which was put into practice by their chief, Marion, on a patient who nearly two years later was still in good health. The continence of the urine is assured by the anorectal sphincter which is subdivided into two passages; one fecal and the end of the intestinal canal, the other urinary constituting a new urethra leading from the newly formed bladder. The rectum is divided above within the pelvis. The upper segment is brought down and invaginated into the primitive anorectal canal, where it will occupy the greater part of the cir-

cumference of this canal, which has been denuded of its mucous membrane, in about the posterior three-fourths of its circumference. Both the upper and the lower segments of the divided rectum will make their exit at the site of the normal anus. The lower segment has been made to represent the bladder, the ureters being implanted into it. Both urinary and fecal canals are then separated, both are accessible externally to the cystoscope, and a valve-like septum exists between the two. The technique of the operation is given in detail and is well illustrated.

The Experimental Production of Basedow's Disease.—BIRCHER (*Zentralbl. f. Chir.*, 1912, xxxix, 138) refers to his previous publication of the results of experimental production of Basedow's disease, in which thymus gland tissue, as fresh as possible, from a thymus hypertrophy or from a patient with a persisting thymus, was implanted in the abdominal cavity. With other authors he had concluded that the thymus gland played an important part in the clinical picture of Basedow's disease, at least as important as that of the thyroid gland. The success of the thymus implantation in his cases was not surprising, he thought, in view of the mortality in the disease, the cure obtained, by Garre with thymectomy, and the symptoms produced by the secretion pressed from the thymus. Bircher is compelled to make this preliminary contribution because of recent antagonistic views. He intends to publish a more extensive paper later. He has produced in five dogs a complete clinical picture of the disease. The pieces of thymus were not obtained from patients suffering from Basedow's disease, but from those who died in shock from thymus persistence (2 cases), or from whom the thymus was removed on account of stenosis. The pieces were fresh and living, being in the air only about a half minute, and were implanted in the abdominal cavity. The results were decisive. In one dog (illustrated) a piece of thymus the size of the palm of the hand and 1 cm. thick, taken from an endemic cretin, was implanted in the omentum. The first symptoms developed in forty-eight hours. The dog was excited, sprang in his cage as if maniacal, took little food and showed much thirst. After four days protrusion of the eyes began to set in and reached its highest point on the twenty-eighth day. It remained stationary some days and then began to subside. It took five months to disappear. The palpebral cleft remained wide and the eyes could not be closed. The upper lid did not follow the eye in looking downward. On the third day tachycardia set in, and quickly reached 180 beats per minute. The jaws showed a rapid fine tremor which also affected somewhat the whole body. The goitre became palpable as a soft tumor after four or five weeks. The tachycardia persisted over three months and can in this dog still be recognized when he is excited. The other symptoms quickly disappeared. Two of the dogs experimented on were allowed to live, in order to study the disease further. Three were killed by a total thyroidectomy. These animals died with a marked tachycardia, with the picture of a quickly developing cachexia strumipriva. The symptoms of Basedow's disease were present in all five dogs in varying degree. Bircher considers that his experiments establish completely the relationship between the function of the thymus and Basedow's disease.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Leukemia with Röntgen Rays.—BIERMANN (*Deut. med. Woch.*, 1912, xxxviii, 7) relates the details of 5 cases of leukemia treated by x-rays. One patient has remained apparently cured for eighteen months. This patient before treatment had a leukocyte count of 450,000, with a hemoglobin percentage of 55, and a red blood count of 2,600,000. Her blood picture and the marked enlargement of the spleen made the diagnosis clearly one of myelogenous leukemia. After the treatment the number of leukocytes was 12,500 and the spleen could no longer be felt. The general appearance of the woman was that of a perfectly well woman, although a differential count showed the presence of a considerable percentage of myelocytis. Biermann believes that myelogenous leukemia, especially in its early stage, is more amenable to x-ray therapy than other forms of leukemia. For this reason he emphasizes the importance of making an early diagnosis of leukemia. Biermann favors gradual and low dosage of the rays and notes briefly his method of procedure in applying this treatment to leukemic patients.

The Use of the Karell Diet in Heart Disease.—His (*Therap. Monats.*, 1912, xxvi, 10) mentions the indications for the Karell milk diet in various circulatory disturbances, and cites cases very favorably influenced by this method of treatment. The Karell "milk cure" is essentially a restriction to a strict diet of 800 c.c. to 1000 c.c. of milk a day, for a period of five or six days. This amount of milk does not, of course, furnish the necessary caloric value for the patient, and the treatment should be carried on only in bed patients. The indications are summed up under a number of different classes of patients: (1) His does not advise the usual Karell cure for cardiac disturbances in obese patients, but only the interposition of an occasional "milk day," as he believes that sudden cardiac weakness may occur if they are kept on too strict a diet for a long period of time. (2) Patients with chronic bronchitis and emphysema associated with increasing weakness of the right heart are much benefited by the Karell treatment. The dyspnea in such patients subsides in a few days on the Karell diet, and longer courses are seldom necessary. (3) Patients suffering from cardiac asthma with degeneration of the myocardium show a rapid improvement of all the symptoms that is often surprising, especially after heart tonics and sedatives have failed to relieve. After a week at most these patients can be allowed a light diet with a limitation of the fluids to 1000 to 1200 c.c., and if necessary the Karell diet may be repeated. (4) True angina pectoris is often remarkably benefited by

this treatment, especially the milder forms, in which the attacks are not severe but are frequently repeated. The results are especially good in plethoric patients with a tendency to meteorism, in whom the anginal attacks are incited by an overloaded stomach or by distended intestines. (5) Insufficiency of the kidneys is known to be benefited by a milk diet, especially when the heart shows signs of weakness, or if there are symptoms of impending uremia. (6) Valvular defects as such are no indication for this treatment, but when the heart muscle becomes insufficient and edema develops, much benefit is obtained by the limitation to the Karell diet. (7) Persistent effusions in the serous membranes often yield quickly to a Karell cure. Von Romberg has recommended the advantages of a salt-poor diet in tuberculous peritonitis. He believes that pleural and pericardial effusions disappear more readily than peritoneal effusions with this method of treatment. (8) This method is of great value as a supplement to digitalis therapy when neither alone is effectual. He cites instances in which digitalis and other diuretics had no effect until after a period of restriction to the Karell diet. In one patient diuresis commenced on the sixteenth day after the restriction to milk, and in another case the diuresis began on the sixth day and did not reach the maximum until the twelfth day.

The Use of Subcutaneous Injections of Heroin in Cardiac Asthma.—FRAENKEL (*Therap. Monats.*, 1912, xxvi, 14) believes cardiac asthma is primarily due to a passive congestion of the pulmonary circulation. This congestion produces an overdilatation of the alveolar capillaries, and consequently a diminution in the size of the alveolar spaces. As a secondary effect of the pulmonary congestion, swelling of the mucous membrane of the finer bronchioles occurs and the lumen of the finer bronchial tubes is often further diminished by spasms of the bronchial musculature. Fraenkel says that morphine acts very favorably upon all these causes of the dyspnea and hence its therapeutic effect in cardiac asthma is usually remarkable. Morphine, however, is open to the objection that it does not act so favorably when its use is long continued. Fraenkel recommends heroin as a substitute for morphine on the ground that heroin has the distinct advantage that it may be given daily for periods of weeks without losing its beneficial effects. The initial dose given by Fraenkel is 0.005 grams, and it may be increased to 0.015 grams. It is often of distinct advantage to combine the heroin with some form of digitalis or other cardiac tonics.

The Action of Iron in Chlorosis.—HEUBNER (*Therap. Monats.*, 1912, xxvi, 44) advances the hypothesis that in chlorosis the ability to reduce the higher salts of iron, the ferric salts, to the lower bivalent forms of iron, the ferrous salts, is lost. The iron in the food is in the form of the higher salts, and chlorotic subjects are not able to assimilate it. He believes that the empiric use of Blaud's pills, of syrup of ferrous iodide, and certain natural mineral waters that contain iron in the bivalent form is justified upon the basis of his hypothesis. The clinical fact that these preparations are particularly useful in the treatment of chlorosis tends to strengthen the theory as advanced by Heubner. On the other hand, the therapeutic effects of iron preparations, such as ferratin, ferrum, oxydatum saccharatum, and hundreds of pro-

prietary preparations have often been disappointing. This, according to Heubner, is due to the fact that these are all the higher salts of iron, and the chlorotic subject is incapable of reducing the iron to a form suitable for absorption.

The Effects of Subdural Injections of Leukocytes on the Development and Course of Experimental Tuberculous Meningitis.—MANWARING (*Jour. Exper. Med.*, 1912, xv, 1) says that cerebrospinal membranes differ from the true serous membranes in that they are almost impervious to blood proteids and normally receive little or no protective substance from this source, and few, if any, leukocytes. Therefore, it becomes necessary to treat pathological processes existing within these membranes by direct inoculation of remedial agents subdurally or into the spinal canal. The author relates his method for producing experimental tuberculous meningitis in dogs and gives a brief summary of the results of subdural inoculations of tubercle bacilli of varying virulence. The leukocytes used in treating the infected animals were obtained by the injection of turpentine into the pleural cavity of dogs, as perfected by Opie in his study of the treatment of experimental tuberculous pleurisy. Manwaring found in his experiments that subdural inoculations of tubercle bacilli of established virulence for guinea-pigs and rabbits produces in the dog a tuberculous meningitis followed by paralysis and death. When suspensions of canine leukocytes are injected subdurally, following such inoculations there occurs uniformly a delay in the development of the paralysis and a prolongation of the life of the treated animal. In dogs inoculated with small doses of tubercle bacilli of low virulence, the development of paralysis has been prevented by this means for periods of seven months (up to the present date), while the untreated animals injected with the same cultures have all developed paralytic symptoms within a period of about four weeks.

Chemotherapeutic Experiments on Animals Suffering from Malignant Tumors.—A. WASSERMANN, HANSEMAN, KEYSER, and M. WASSERMANN (*Berl. klin. Woch.*, 1912, xlix, 4) relate their experiments in an endeavor to find a chemical substance capable of exerting a specific destructive action upon the cells of malignant tumors occurring in mice either spontaneously or as a result of inoculation. They found in experiments in vitro that selenium and tellurium salts were taken up selectively by carcinoma cells. They also found that when salts of selenium and tellurium were injected locally into the tumors of mice affected with carcinoma these tumors softened and liquefied. However, it is not possible to inject all malignant tumors locally, and any attempt to cure a malignant tumor must take in consideration the possibility of reaching all the tumor cells that possibly may be distributed by metastases widely throughout the body. They next attempted to find some chemical preparation derived from these metals that could be injected into the blood, and that would distribute itself rapidly throughout the body and at the same time be diffusible. More than 200 chemical combinations were tried before Wassermann and his co-workers obtained a preparation consisting of a compound of eosin and selenium. This chemical combination is unstable, and the exact

nature of it is not given. This substance is a red powder very easily soluble in water. After injections of this solution into the caudal vein of mice there occurs almost immediately a diffuse reddening of the entire animal that usually disappears within twelve hours. The injections were given daily and after the third injection a distinct softening of the tumor was evident on palpation. After the fourth injection this softening was more evident and the formerly solid tumor now appeared to be a fluctuating cyst. The injections were continued, and usually in ten days a complete disappearance of the tumor was noted. The injections, however, did not always lead to this favorable result, as many of the animals died after the first, second, or third injection. This result may have been due to improperly prepared preparations. Mice with large tumors frequently become severely poisoned when liquefaction and softening of the tumor occurred rapidly. The authors are of the opinion that these toxic symptoms are due to the absorption of the destroyed tumor. The animals in whom the tumors healed have remained without recurrence for months. They conclude from these experiments that it is possible to cure malignant tumors in mice by this means provided the tumors are not too large in proportion to the body weight of the animal. They wish to warn that there is no evidence that eosin-selenium will act similarly with human cancer. However, their experiments do point out a line of investigation that may be extended and lead to a progress in human therapy.

Hexamethylenamin in the Treatment of Bronchitis.—VANDERHOOF (*Jour. Amer. Med. Assoc.*, 1912, lviii, 331) recommends hexamethylenamin as a remedy of great value in cases of acute colds and in patients suffering from acute and chronic bronchitis. The drug should be given in large doses accompanied by the copious drinking of water. In the ordinary cold, treatment with hexamethylenamin shortens the stage of coryza and greatly modifies or entirely prevents the succeeding bronchitis. He also believes that it acts as a prophylactic against ensuing infection of the accessory nasal sinuses. Vanderhoof says that it is our best remedy in acute bronchitis. Certain cases of chronic bronchitis respond to treatment by hexamethylenamin with a gratifying alacrity, while others do not. In the latter instance it is presumed that structural changes have occurred in the walls of the bronchi, associated with thickening and calcification of the cartilages, fibrous membrane, and muscular coats so as to preclude the hope of successful treatment by any remedy.

Salvarsan in Syphilis of the Nervous System.—SACHS and STRAUSS (*Med. Record.*, 1912, lxxxi, 211) have used salvarsan in 80 cases of syphilis of the nervous system, and conclude that salvarsan has no curative effect in tabes and general paresis. Salvarsan seems to influence favorably some of the symptoms particularly the vesical and sexual functions, and under its use some of the cases remained stationary. None of the patients treated with salvarsan exhibited any unfavorable symptoms attributable to the drug itself. They believe that in these two diseases it accomplishes as much as, but not any more than was achieved in former years by the use of mercurials. In brain and

spinal cord syphilis the use of salvarsan is followed by an improvement in many of the symptoms, but they do not believe that the results obtained with it have been better than those obtained by mercury. In the acute and subacute form of brain syphilis, especially when associated with convulsive seizures and with chronic headaches, the drug has been distinctly beneficial. Without doubt the good effects of this treatment may be made more lasting by the additional use of mercury and the iodides. Although their results were negative with its use as a therapeutic agent, yet they hope that the use of salvarsan in the early stages of syphilis may prevent the development of late and more serious forms of specific disease of the central nervous system.

Personal Experiences with Digipuratum.—BREITMAIER (*Deut. med. Woch.*, 1911, xxxvii, 2376) recommends digipuratum as a substitute for digitalis extracts and tinctures. He believes that it is much less apt to vary in strength than other digitalis preparations, and that it does not deteriorate with age. He believes that the absorption and elimination of digipuratum are more rapid than other digitalis products, and therefore cumulative action of the drug is less likely to recur. Digipuratum also causes less digestive disturbances, due to the fact that certain irritating elements that occur in other digitalis preparations have been removed. It has the additional advantage that it can be given intravenously.

Digitalis Preparations Employed in Medicine.—DIXON (*Quart. Jour. Med.*, 1912, v, 297) reviews the findings of many observers on the action and effects of the different digitalis preparations employed in medicine. The three principal glucosides of digitalis leaves are digitoxin, digitalin, and digitonin. He describes the properties of these three glucosides briefly. Digitonin is a saponin found principally in digitalis seeds and has no value as a cardiac tonic. It is soluble only with difficulty in cold water but is much more soluble mixed with digitalin. It is owing to the presence of digitonin in digitalis leaves that digitoxin and digitonin find their way into the watery preparations, such as the infusion. Digitalin has an effect on the heart similar in the main to digitoxin, but is only about half as active. Digitoxin is the most active constituent of digitalis leaves. Its insolubility renders it difficult to deal with; it is very irritant, and if given by the mouth causes gastric symptoms more than any other digitalis preparation. The subcutaneous administration of digitoxin causes severe pain, and it may induce necrosis and suppuration. It is slowly absorbed and is still more slowly eliminated, and therefore has a cumulative effect. One great object in preparing substitutes for the galenic preparations of digitalis has been to obtain a form suitable for subcutaneous injections. Another objection to the use of the ordinary preparations of digitalis is the fact that the therapeutic effects, especially the diuresis, do not appear before the second day, and more commonly on the third day, and this renders the drug of little value in acute conditions, and when an immediate action is required. Dixon describes briefly the three most important proprietary preparations which have been introduced to meet the disadvantages of the ordinary digitalis preparations. Digalen or soluble digitoxin was first prepared by Cloetta, who

claimed for it a superiority over digitoxin, in that it was soluble in water, less irritant to the stomach, more constant in strength, more rapid in its action, and, lastly, that it was not cumulative like digitoxin. Dixon cites the widely opposed views of different observers regarding these advantages claimed for digalen. Clinicians vary in the widest degree in reports as to its clinical value. Some think it is an ideal digitalis preparation, while others regard it as most unsatisfactory. Digalen is probably not so irritant to the stomach and alimentary canal as digitoxin. Subcutaneous injections of digalen are very painful and frequently produce inflammatory reactions. The consensus of opinion is that it is not more rapid or constant in its action than a properly standardized tincture and has also a distinct cumulative action. Digipuratum is a preparation made from digitalis leaves by exhausting them with alcohol and ether. By this means it is stated that 85 per cent. of the inert material in digitalis leaves, including the saponins, is removed and that the remaining 15 per cent. contains all but a small percentage of the active constituents. The four virtues which can be assigned to digipuratum are that it keeps well, it is uniform in composition, it contains all the glucosides of value in digitalis, and causes less gastric irritation than the powdered leaves. The one great disadvantage is that it is ten times more expensive than the tincture of digitalis, and Dixon says that a properly standardized tincture of digitalis has all the advantages of digipuratum. Clinical reports on digipuratum are on the whole very favorable. Digitalone, like digalen and digipuratum, has a typical digitalis action on the heart, and it is claimed for this preparation by the manufacturers that it is suitable for oral, hypodermic, intravenous, or rectal administration. Dixon does not believe that the action of digitalone differs from the ordinary galenical forms except that it is less active. In conclusion, it may be stated that pharmacological and clinical investigations have not made a clear case for the substitution of active principles for galenical preparations of digitalis in the treatment of patients. These active principles are for the most part just as irritant as the infusion or tincture; they are neither more reliable and constant in action than a properly standardized tincture, nor are they absorbed more rapidly; they have the same tendency to accumulate and are much more expensive. The one advantage that certain of them may possess over the pharmacopoeial preparations is that they may be given intravenously without ill effects.

The Treatment of Syphilitic Heart and Vascular Disease.—OIGAARD (*Zeit. f. klin. Med.*, 1911, lxxiii, 440) says that the Wassermann reaction is of great value as an aid to the diagnosis of syphilitic aortitis that is in many cases difficult to diagnose clinically. Aneurysm of the arch of the aorta and aortic insufficiency are almost always of syphilitic origin and the Wassermann reaction is usually positive. Mercurial treatment was given to the patients reported by Oigaard with very good results. He also tried iodides but does not believe they have any effect upon the course of the disease. The mercurial treatment should be continued until the disappearance of all subjective symptoms, and until the positive Wassermann reaction becomes negative. Treatment should be resumed upon the recurrence of any subjective symptoms or a return to a positive Wassermann reaction.

PEDIATRICS

 UNDER THE CHARGE OF

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The Therapy of Tuberculous Ascites in Children.—MAX KLOTZ (*Berl. klin. Woch.*, 1912, xlix, 73) points out that the withdrawal of the ascitic fluid by paracentesis in tuberculous peritonitis, is not always dangerous or useless. Out of 11 cases he mentions 5, in 2 of which a single tapping was sufficient to permanently cure the ascites. Two cases required two tapplings to accomplish this, and 1 case required four tapplings. The indications for tapping in this condition are, when there is an increase in, or no decrease of, the ascites after rest in bed, dieting, sun baths, food poor in salt and diuretics. If the fluid returns another tapping is indicated. If there is no return of fluid in fourteen days the patient is allowed to sit up one hour at a time, gradually increasing the periods. Klotz has seen no bad effects occurring from this plan of allowing the patient to sit up, although a number of authorities make a point of long continued rest in bed. Klotz has seen the return of the ascites under this latter method. The length of the treatment varied from five to nine months. Five out of 11 cases are clinically cured or well after nine to twelve months from their discharge. One child had an exudative pleurisy complicating the ascites. Tuberculin, tried in 2 cases, showed some improvement in 1 case, and had no effect in the other. The acholic stools which Berggrun and others hold as of diagnostic value were not seen in any case of tuberculous ascites. Infiltration of the umbilical region, which Schmidt found in 7 per cent. of his cases, is rare, and occurred but once in the 11 cases of Klotz. Klotz claims that in general practice good results can be obtained by any physician who employs the hygienic and dietetic treatment given above and performs paracentesis under the above conditions and rules.

The Prognosis in Epilepsy in Children.—JULIUS ZAPPERT (*Med. Klinik.*, 1912, viii, 229) calls attention to the difficulty of prognosis in the epilepsy of children, a condition in which the diagnosis alone offers great difficulties. Besides excluding hysterical attacks and the convulsions of childhood there remain doubtful cases with pronounced epileptiform convulsions which cannot be pronounced true epilepsy. Also in cases giving the picture of uncomplicated true epilepsy, a subsequent change in the symptom-complex is possible, so that the rule may be laid down that in childhood these cases should be diagnosticated as epileptiform attacks and not as true epilepsy. While a large number of cases with typical attacks in early childhood subsequently develop severe and permanent epilepsy, there remains quite a number of cases in which typical attacks occurred frequently for from one to three years and then diminished and disappeared altogether without subsequent return to date. Zappert gives short histories of 7 such

cases. These cases were almost invariably boys and the attacks were typical of epilepsy. Another type exhibits typical attacks associated with reflex irritation from intestinal parasites, the attacks ceasing with the discharge of the parasite. Again, in cases of so-called spasmodic or idiopathic eclampsia in childhood, Birk and others claim that a certain number develop true epilepsy in adult life, while Hochsinger claims there is no genetic relation between the two conditions. Zappert details a number of cases which gave typical attacks associated with symptoms of pseudobulbar palsy. These attacks lasted from one to two years and the prognosis was bad. However, under treatment with bromides the attacks ceased and have not recurred. Here we have the possibility, however, of their reappearance at some future time. In the prognosis of epilepsy it must be remembered that severe and incurable diseases of the brain often stand back of the attacks. There are many cases in which the diagnosis of epilepsy can be made with a high degree of certainty, and which, even after sedative treatment is stopped, show improvement and an absence of symptoms for one or more years. It seems proper to offer a milder prognosis than heretofore in the epilepsy of childhood, and hold out at least the probability of a cessation of the attacks for a long time, and the possibility of a spontaneous cure.

The Influence of Heredity on the Development of Cardiac Disease.
—MAX HERZ (*Münch. med Woch.*, 1912, lix, 419) believes that more weight should be placed on the influence of heredity on the development of cardiac conditions. The results of this influence in a number of cases has been of great significance in the differential diagnosis, and especially in the prognosis, of cardiac conditions. Herz briefly outlines from his experience the influence of heredity in the three chief groups of cardiac affections, namely, the neuroses, the rheumatic, and the arteriosclerotic conditions. The simultaneous appearance of a nervous cardiac affection in parents and their children is a common observation. Especially frequent is a nervous extrasystole in children of neurotic parents. The frequent occurrence of articular rheumatism, chorea, and the attendant cardiac lesions in families is well known. A predisposition for this condition cannot be doubted. In the majority of cases the child inherits this predisposition from the mother. The above facts become of significance in determining whether a cardiac murmur in a child is due to valvular disease or not. In doubtful cases it is better to accept as functional a cardiac murmur in a child between six years and puberty, since experience shows that in most cases the murmur will disappear during puberty. However, if the child's mother presents the stigmata of a rheumatic constitution, the prognosis should be decidedly more guarded. The clearest and most impressive influence of heredity, however, is found in the condition of sclerotic cardiac disease. Sudden death from cardiac failure at a certain age is especially common in some families. This occurs usually from the fortieth to the sixtieth year. In connection with nervous cardiac affections the element of imitation or mimicry is a factor not only in cases of children imitating the symptoms of cardiac neuroses in their parents, but also in cases of susceptible attendants or nurses in cases of organic cardiac disease.

O B S T E T R I C S

UNDER THE CHARGE OF

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The Pathogenesis of Hemorrhage in the Newborn.—BONNAIRE and DURANTE (*L'Obstétrique*, October 10, 1911) report 4 cases of fatal hepatic hemorrhage, non-traumatic, in newborn infants, accompanied by considerable bleeding into the peritoneal cavity. They analyze these cases in detail, and come to the conclusion that under the influence of an intoxication or a chronic infection in the mother, vascular lesions and cellular degeneration in the liver develop in the infant, diminishing the formation of fibrinogen and causing a deficient power of coagulation in the child's blood. At the moment of birth the intoxication or infection produces a polyglobular condition in the infant, with excessive leukocytosis and congestive phenomena. The blood-vessels are disordered and the capillaries altered by the cellular degeneration in the parenchyma of the organs. In a child previously healthy the traumatic lesion producing rupture of the vessels might end in recovery; but in these cases hemorrhage occurs in the parenchyma of the liver or beneath Glisson's capsule, causing distention and the final extravasation of blood in the peritoneal cavity. The reviewer has recently seen two cases of this condition. In one, a comparatively young woman, there was chronic catarrh of the bile ducts, and when in the non-pregnant condition she suffered repeatedly from biliousness and jaundice. After easy parturition she lost two apparently well-nourished infants, the first from intestinal hemorrhage; the second from diffuse pulmonary hemorrhage. In the latter a thorough autopsy demonstrated multiple hemorrhage into the parenchyma of the liver, and a bacillus was isolated from the blood and tissues of the infant. The mother has been urged to submit to a cholecystotomy and thorough drainage of the gall-bladder. This advice has not been accepted, but she has compromised by a Carlsbad cure. The second case, a primipara, older than the average, disregarded hygienic precautions in her diet during pregnancy, and lost her infant from hepatic bleeding.

Postoperative Thrombosis and Embolism.—KLEIN (*Monats. f. Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 5) gives the results of his studies on this question over a period of twelve and one-half years. Most of the cases studied were those of gynecological operations, although there were among these some cases of general surgery, such as extirpation of the breast for carcinoma, operations for hernia, appendectomy, and other operations on the intestine. Cases of confinement and the puerperal period are not included in this report, and cases of endometritis preceded by abortion are also omitted. The total number of operations is 5524, with 50 cases of thrombosis and embolism, *i. e.*, 0.9 per cent. In 1720 laparotomies there were 29

cases of thrombosis, or 1.7 per cent. The former belief was that thrombosis and embolism depended upon the nature of the patient's illness and the sort of operation. More recent knowledge indicates that thrombosis is dependent upon physical reasons, and that alteration in the blood and slowing of the circulation are important factors in the case. Such diseases as uterine myomata, often accompanied by degeneration of the heart muscle, predispose to this accident. It is also true that the more serious the operation, the greater the liability, and that more cases of laparotomy have this accident than of less severe operations. Thrombosis and embolism is most frequent after abdominal section for the removal of myomata. In comparing abdominal section with vaginal section, he found, in 1720 abdominal sections, that there were 29 cases of thrombosis, or 1.7 per cent.; while in 1992 vaginal sections there was but 0.8 per cent. of thrombosis, or not quite one-half in abdominal section for myomata. Whether supravaginal amputation or total extirpation was performed the number of cases of thrombosis was three times as great as after vaginal operations for the removal of myomata. The most serious result of thrombosis is fatal embolism. In the 1720 abdominal sections there were 9 cases of fatal embolism; while in 1992 cases of vaginal section there was none. The vaginal operations were quite as severe as those performed through the abdominal wall. There seems to be an important advantage in the advantage of the vaginal method of operating. Thrombosis after operations on the adnexa is not rare. Most of these cases were not those of inflammatory disease, but of primary tumor of the tubes or ovaries. In 1905 operations upon the adnexa, there were 11 cases of thrombosis, or 1 per cent., and 2 fatal cases of embolism. One of these was after removing a carcinoma of the left ovary. After a radical abdominal operation the patient did well until the ninth day, when thrombosis in the left leg appeared, followed shortly after by fatal pulmonary embolism. The patient was extensively diseased in many ways. The second case was that of a woman aged forty-eight years, operated upon for hydrosalpinx and cystic ovary of the right side. On the fifth day after matters were apparently going well, there was fatal pulmonary embolism. Thrombosis was rare after operations for prolapse and retroflexion, but after curetting for hemorrhagic endometritis the accident occurred on the fifth day. When the age of the patients is considered, 52 per cent. of all cases were in middle life, between forty-one and fifty-one years. The youngest woman was aged nineteen, the oldest sixty-seven years. In 38 cases one could detect the beginning of the thrombosis, and the greater number happened between the first and tenth days after operation; and an almost equal number between the eleventh and twenty-first days. Most of the cases occurred in the first three weeks after operation. The majority of the cases occurred on the left side of the pelvis and in the veins of the left thigh. In 44 patients there were 24 cases on the left, 11 on the right, and 9 on both sides. Most cases of embolism are pulmonary, and in 13 cases 10 were of this nature. There was one apoplexy, where after thrombosis of the left crural and iliac veins an embolus found its way to the fissure of Sylvius. These cases seemed more common after operations for carcinoma. In classifying operations, every case in which the uterus was extirpated was considered a

radical operation. One of these, followed by fatal embolism, was done for eareinoma. In 41 radical operations for carcinoma there were 16 abdominal sections, and 25 vaginal sections, in a total of 563 operations for carcinoma; 0.2 per cent. of these had thrombosis. In searching for a cause for this accident, one naturally turns first to the possibility of an infection in the blood. If we are to diagnosticate this by a rise in temperature, such a condition was absent in 14 cases, which is 28 per cent. of all the cases of thrombosis. Direct infection of the wound could be traced in 8 cases, or 16 per cent. In these cases there was either abscess in the abdominal wall, or suppuration in the vaginal wound. Other causes are those mechanical factors which disturb greatly intra-abdominal pressure, such as large tumors in the pelvis in 7 cases, ascites in 3 cases; marasmus and anemia in 1; pernicious anemia in 14; insufficiency of the heart's action in 12; arteriosclerosis in 2; bruising of the vessels by mass ligatures or resections of large veins, in 4 cases; prolonged anesthesia in 6; varices in 4; and other conditions affecting the general health. All of these tend to alter the constitution of the blood, disturb blood pressure, and retard circulation. To avoid this accident one should guard carefully the strength of the heart muscle, if necessary giving digitalis for some time before operation, and when circumstances are favorable avoiding delay, because of its depressing influence. It is thought that lumbar anesthesia is less dangerous than that by inhalation. Strict asepsis, avoidance of mass ligature, and wounding of the large veins should be observed, and, if possible, the avoidance of chill on the skin of the abdomen. After operation the patient should receive nutritious foods in great abundance, and if necessary the circulation should be promoted by massage or passive movements. The comparative frequency of this accident is studied by quoting the reports from various clinics, aggregating between 30,000 and 40,000 operations. The frequency of the accident varied from 3.6 per cent to 1 per cent.

The Sterilization of the Skin.—LEEDHAM-GREEN (*Brit. Med. Jour.*, October 28, 1911) has made culture experiments with various strengths of iodine, with alcohol, and with sublimate alcohol, in sterilizing the skin. Although a final conclusion has not been reached, the experiments so far may indicate a slight superiority in sublimate alcohol over iodine, than alcohol alone. When sublimate alcohol and iodine were merely painted on the skin there was little difference in the result; but when sublimate alcohol was thoroughly rubbed into the skin it proved in the majority of cases more efficient. The sublimate solution used was 1 to 1000 in 70 per cent. alcohol. This was compared with 70 per cent. official tincture of iodine and 1 to 1000 aqueous solution of bichloride of mercury. The result was in favor of the 70 per cent. sublimate alcohol.

GYNECOLOGY

 UNDER THE CHARGE OF

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Anatomical Cure of Cystocele.—WHITE (*Amer. Jour. Obst.*, 1912, lxxv, 286) does not believe that any of the commonly accepted theories as to the pathological anatomy of cystocele are correct, and thinks that the unsatisfactory results obtained in its treatment are due in large measure to a faulty conception of the cause. His studies on the cadaver have convinced him that the bladder stays in place because it rests on a firm fibrous shelf, which stretches across between the pubic bones from the symphysis to the spines of the ischium, this shelf being nothing more than the anterior vaginal wall, which is attached by firm adhesions to the pubic bone in front, and laterally to the whole length of the white line of the pelvic fascia. This can be easily demonstrated by running a knife along the white line on either side and severing the attachments to the vagina; a cystocele of marked degree will be produced. Upon suturing the vagina back to the white line, normal conditions are restored, and the cystocele is cured. Acting upon this theory, White has devised the following operation. An incision is made in the anterior lateral fornix of the vagina, extending from the level of the cervix to near that of the internal meatus of the urethra. The finger is then worked by blunt dissection toward the side of the pelvis until it can be placed on the uncovered ischiadic spine. By means of a curved needle three or four sutures are then passed through the lateral edge of the vaginal incision, around back of the white line, and out through the mesial edge of the vaginal incision; when these are tied the lateral fornix of the vagina is drawn up into contact with the white line. The other side is treated in the same manner, so that at the completion of the operation the anterior vaginal wall stretches across from one ischiadic spine to the other, reestablishing the normal shelf-like condition. The operation sacrifices no tissue, and in the author's experience has given most satisfactory immediate and remote results.

Etiology of Appendicitis.—Excessive eating, especially of red meats, is an important factor in the causation of appendicitis, according to DICKINSON (*Amer. Jour. Obst.*, 1912, lxxv, 284), who calls attention to the fact that man is the only animal that suffers from this disease, and that he is the only one that makes eating a pleasure, filling his intestinal tract with high proteids, the undigested portions of which undergo fermentation. It is also worthy of note in this connection that physicians working in China, where red meat is very little eaten, report rarely seeing a case of appendicitis among thousands of patients examined. Dickinson believes, therefore, that there is a close connection between gluttony and the disease, but also lays emphasis on the

importance of the condition of drainage in the appendix in determining the type. He distinguishes between the progressive, destructive form, and the chronic hyperplastic, which goes on to fibrosis. In the former the ceco-appendicular junction is tubular, the lymphoid tissue at the junction being so swollen as to choke the aperture, so that the appendix cannot drain itself; this results in tension, leading to gangrene or perforation. In the chronic or hyperplastic type the ceco-appendicular junction is funicular, embryonal in character; drainage is good, and tension does not occur. The sequence of events is therefore probably somewhat as follows: overeating of high proteids, residuum in cecum, decomposition, ceco-appendicitis. The cecum, draining well, recovers; the appendix, if not draining at all, goes on to destruction; if draining poorly, to subacute appendicitis with hyperplasia; if draining well, to chronic appendicitis with fibrosis.

Conservative Surgery of the Ovaries.—DICKINSON (*Surg., Gyn., and Obst.*, 1912, xiv, 134) has studied the results in a series of 131 operations performed on intelligent women from private practice. All these were done more than six months ago, this arbitrary time-limit having been chosen because symptoms of the surgical menopause generally develop within this time if at all. In 80 per cent. of the cases in which one or both ovaries were left, no climacteric disturbances of any kind occurred. The failure to prevent these entirely in the remaining fifth of the cases may have been due, Dickinson thinks, to lack of skill or care in preserving the ovarian circulation. He believes that this is better accomplished by leaving the tubes as well, when they are healthy, as important nerves and arteries going to the ovary may be cut in removing them. His doctrine is that all healthy ovaries should be left in place, even if the patient is near the menopause, since no one can say just what is the term of ovarian activity, and especially is this true in fibroid cases, in which the ovary is notoriously long-lived. Dickinson believes that better results are obtained when both ovaries are left than when one is removed, or resections are done. He has found that, as far as can be determined, conservation in married women is followed by persistence of sexual desire in almost all cases. The question of leaving or removing ovaries in operations for advanced inflammatory disease is often a very difficult one to decide, as these ovaries are apt to be very tender, and to give rise to trouble later; Dickinson says that he is, therefore, rather inclined to remove them under such circumstances, unless the patient is fairly young and vigorous, and there seems to be no infection of the ovary.

Post-climacteric Metrorrhagia of Non-cancerous Origin.—DALCHÉ (*Gaz. des Hôp.*, 1912, lxxxv, 3) calls attention to the fact that not all uterine hemorrhages occurring after the menopause are due to malignancy, and that although we should never lose sight of the overwhelming importance of this etiology, neither should we overlook the fact that certain of these cases are amenable to medical treatment, or undergo spontaneous cure. Sufferers from an old metritis, following frequent childbirths, and accompanied by a general visceroptosis, are frequently the subjects of severe post-climacteric hemorrhages. These may likewise occur, often associated with a profuse, fetid discharge,

as a result of senile metritis, the condition clearing up entirely after a simple dilatation of the cervix and intra-uterine lavage. Mucous polyps and fibromyomas are well recognized causes of post-climacteric bleeding, which may be very severe and intractable even in cases of but a single small submucous nodule. A condition, however, which in Dalché's opinion is not thought of nearly often enough as the etiological factor in these cases is syphilis. This may manifest itself as a diffuse syphiloma, forming a large uterine and peri-uterine mass, as multiple gummas, forming a friable, nodular mass on the cervix, or merely as a sclerotic condition of the uterus and its vessels, all these conditions giving rise to metrorrhagias, and all being cured by specific treatment. It should not be forgotten, moreover, that post-climacteric bleeding may in some instances be due to an actual return of menstruation, corresponding to a tardy ovulation. Finally, such hemorrhages may be due to extragenital causes altogether, such as endo- and myocarditis, hepatic or renal diseases, lumbo-abdominal neuralgia, and obesity. All these conditions may be accompanied by metrorrhagia, whose cause is to be sought outside of the genital sphere.

True Bone Formation in the Tubes and Ovaries.—Four cases of this exceedingly rare condition are reported by Pozzi and BENDER (*Rev. de gyn. et de chir. abdom.*, 1912, xviii, 129), 2 of these affecting the tube and 2 the ovary. After a most careful analytical study of the literature Pozzi and Bender were able to find but 5 additional cases of true ossification in the ovary, and but 2 additional cases in the tube. They conclude from the study of their own cases and of those from the literature that the process is identical, whether its seat be in the ovary or the tube. These studies have shown the fallacy of the older theory that development of osseous tissue in the ovary is inseparable from the existence of a teratoma or dermoid cyst, as there were no traces of anything of the sort in their specimens. What is the significance of this intrinsic, true ossification of the ovary and tube? It is not a neoplastic process, hence the term "osteoma" is inappropriate. Pozzi and Bender believe that the osteogenesis, which is always decidedly limited in extent, is a regressive modification of pre-existing tissue elements. The ossification is always preceded by calcification. Histologically actual bone tissue was found in all the cases, with osteoblasts and marrow tissue, the latter containing all the cell-types found in normal marrow. In no case was cartilage found, so that the ossification cannot be considered as having occurred from aberrant cartilage rests. In some instances a direct metamorphosis of fibrous tissue into bone had occurred, such as is seen in the formation of the membrane-bones of the skull; in other cases calcification had evidently taken place, followed by irritation, this causing proliferation of connective tissue, with the formation of myeloid tissue containing osteoblasts, these then causing the bone formation. According to these observations bone formation in the tubes and ovaries, although occurring very rarely, follows exactly the same laws that govern heterotopic osteogenesis in other portions of the body.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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The Influence of Sterile Environment, Inspired Air, and Food on the Digestion and Metabolism of Animals.—KIANIZIN (*Jour. de Physiol. et de Path. gén.*, September 15, 1911, xv) placed experimental animals in a sterile bell jar through which sterilized air was circulated. The sterilization of the air was controlled by drawing it, before its passage into the bell jar, through sterile broth. The broth remained clear throughout the experiments, so that there is little doubt but that the air was freed of microorganisms. The animal under observation in the bell jar was placed on a shelf composed of close-meshed wire netting. The excrement dropped through this netting into a strong solution of boric acid. The urine was collected separately. The total nitrogen and the relation of the nitrogen of the urea to total nitrogen was studied, and the ratio of the nitrogen of the urea to total nitrogen was taken as an index of the metabolism. These experiments in each instance showed a reduction in the ratio between urea nitrogen and the total nitrogen, but this reduction in no instance was very considerable. Folin has shown that this ratio between the nitrogen of the urea and the total nitrogen may undergo considerable variation in normal adults upon a mixed diet, so that the relatively slight changes in the nitrogen ratio mentioned by Kianizin are not to be regarded as proving absolutely that bacteria, which ordinarily are present in the air and the food, are absolutely indispensable for the life of the organism. It should be stated that many of the experimental animals died rather quickly. Kianizin did not believe that the cause of death in these cases was due wholly to digestive troubles; he believed that they were caused by an intoxication due to modifications of metabolism. The experiments, while very suggestive, are not conclusive.

The Hygiene of the Swimming Pool.—JOHN W. M. BUNKER (*Amer. Jour. Pub. Hyg.*, November, 1910, xx,) and WHIPPLE and BUNKER (*Eighteenth Annual Convention of the American Society of Municipal Improvements*, 1911) have studied the effects of "bleach" (calcium hypochlorite) in purifying the water of swimming pools. Chemical analyses have shown that the water of swimming pools becomes polluted, the degree of pollution depending largely upon the number of persons bathing in the pool. This pollution is shown by an increase in the amount of free ammonia, albuminoid ammonia, and by a decided increase in the number of bacteria. It is a curious fact that the numbers of *Bacillus coli* are not increased as markedly as might be expected. In a series of experiments, which are recorded, the colon bacillus is

uniformly absent in 0.1 c.c. of water from the swimming pool even after ten days, but is irregularly present in 1 c.c., and quite generally present in 10 c.c. In one experiment the bacteria growing on gelatine at 20° C. increased in numbers from 205 per cubic centimeter to 255,000 in three days, and to 281,000 in four days. After using "bleach" in the proportion of 1 part per million, these numbers were reduced very materially. Thus, a sample of water obtained from the new swimming tank in Brown University showed an original bacterial content of 700 c.c., and this was reduced to zero in fifteen minutes following the addition of the hypochlorite. A similar experiment carried out in the tank itself gave somewhat similar results. Surface samples before the addition of "bleach" yielded a count of 500 bacteria per cubic centimeter. Fifteen minutes after adding one-half a part of bleach per million of water these bacteria were reduced from 700 to 30 per cubic centimeter, and after thirty minutes to 10. At the end of an hour the water was sterile (*i. e.*, no colonies on plates). A sample taken eight hours later, while the pool was still agitated from those who had bathed in it, showed a bacterial content of 5 per cubic centimeter. The pool remained practically sterile for four days, at the end of which time the bacterial count began to rise steadily. It would seem that the application of hydrochlorite of lime offers a cheap, efficient, and convenient method of keeping the number of bacteria in a swimming pool down, and this diminishing the potential danger incident to bathing in a common tub.

The Etiology and Transmission of Measles.—ANDERSON and GOLDBERGER, in a series of articles (*Public Health Reports*, June 9, 1911, xxvi, 847; *Ibid.*, 887; *Jour. Amer. Med. Assoc.*, July 8, 1911, lvii, 113, 114; *Ibid.*, August 5, 1911, lvii, 476 to 478; *Ibid.*, 971, 972; *Ibid.*, 1612, 1613) have reported the results of their experiments upon the etiology and mode of transmission of measles. In the first paper by these authors they report upon the susceptibility of the rhesus monkey to inoculation with blood from human cases of measles. Previous to their work it had been generally accepted among laboratory workers that monkeys were not susceptible to the disease. In their third paper Anderson and Goldberger show that the apparent non-susceptibility of the monkey to infection with measles was due to a more or less limitation of the period of infectivity of the blood, beginning at least several hours before, and continuing for about twenty-four hours after, the first appearance of the eruption. At the end of twenty-four hours from the first appearance of the eruption the infectivity of the blood for the rhesus monkey becomes greatly lessened and becomes progressively less thereafter. They draw attention to the fact that this limited period of infectivity also throws much doubt upon the value of previous bacteriological studies of the blood in measles, as it is quite possible that many workers have used non-infective blood. The fourth paper is on the nature of the virus existing in the circulating blood. They found that in a certain proportion of cases the measles virus in the blood is capable of passing through a Berkefeld filter. It resists drying for at least twenty-four hours. The infectivity of the defibrinated blood is destroyed by heating to 55° C. for fifteen minutes; and the defibrinated blood frozen for twenty-four hours is still infective at the end of that time. They were able to pro-

duce the disease in monkeys by placing them in a cage with sick monkeys during at least the early period of the disease. It was found that the incubation period of measles contracted in this way was not more than eleven days nor less than five. In a fifth paper they report on the infectivity of the nasal and buccal excretions from human cases of the disease. They found that the nasal and buccal secretions collected within the first forty-eight hours after the appearance of the eruption were infective for monkeys inoculated subcutaneously with this material. In a sixth paper they report on the duration of the infectivity of the secretions. Their results suggest strongly a reduction, if not a total loss, of infectivity of the nasal and buccal secretions in human cases of measles with the approach of convalescence. They tested out the infectivity of the measles scales and found, in six experiments, that in no instance were the scales infective. These studies by Anderson and Goldberger on the mode of transmission and etiology of measles virus is our first definite knowledge based on laboratory experiments as to the susceptibility of the monkey to inoculation with blood from cases of measles. They prove conclusively the infectivity of the nasal and buccal secretions during at least the first forty-eight hours of the eruption, and their experiments all tend to support their opinion that the scales in measles are non-infective. While Anderson and Goldberger are conservative in drawing their conclusions as to the duration of the infectivity of the secretions, their results are in accord with clinical observations that cases of measles are not infective after convalescence, which fact seems now to be well established. The importance of this latter point from a public health standpoint can be readily appreciated, for it has been the custom where quarantine is required for measles that the quarantine be maintained for twenty-one days from the onset. Based on the experiments of Anderson and Goldberger, it would seem that this period of quarantine can be safely reduced to ten days from the onset, as convalescence is usually well established in uncomplicated cases by that time.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Experimental Teratoid Tumors.—Two communications of much interest relative to the experimental causation of teratoid tumors were made at the International Pathological Congress at Turin. BORST (*Centralbl. f. allg. Path. u. path. Anat.*, January 15, 1912, xxiii, No. 1) reported 74 per cent. of successful inoculations of embryo emulsion, intraperitoneally, in white rats. Females were more readily inoculated

than males, although age was of little importance; the gravid state assisted the development of the tumors. Some "growth-stimulating" substances such as ether and indol used upon the emulsion, and in some cases injected after the tumors had begun to grow, proved ineffective in Borst's hands. Subcutaneous inoculation was unsuccessful, and animals in which this had been tried could be successfully inoculated afterward in the peritoneum. In addition to the tissues usually seen in such tumors the author has found brain-substance, lung, and spleen tissue. There was evidence in favor of autogenous formation of vessels, and of junction of such vessels with those of the test animal. ASKANAZY (*Ibid.*), who has priority in this work, reported further observations on the effects of "growth-stimulating" substances, used upon the embryo emulsion and also upon the test animal, and admitted that the results had scarcely come up to expectation. After subjecting the emulsion to ether solution and vapor for a day, 2 animals out of 8 injected subcutaneously showed growths of osteosarcomatous nature, both animals dying in the same length of time, these 2 being the only cases of malignant tumors seen in hundreds of animals observed. It certainly might be deduced that a heightening of the potency of growth of the cells had been obtained. The x-rays have a restraining action upon the potency; alcohol and lipase gave marked increase of growth, as did chloral hydrate, probably by inducing a cell-narcosis in the host-tissues. One animal so treated developed a large epithelioma. The presence of cartilage bone, glia, etc., speaks for the teratogenous nature of such a carcinomatous growth, but the question is still to be answered whether the malignant growth is essentially from the inoculated tumor or is a reaction on the part of the host-tissues. The extirpation of various organs has been practised and its effect upon teratoid growth observed; castration was of no effect; when the spleen was extirpated at the time or before the inoculation of 9 animals, 6 gave no tumor formation and 3 others but an insignificant degree.

The Bacterial Cause of Typhus Exanthematicus.—FUERTH (*Zeit. f. Hyg. u. Infekt.*, 1912, lxx, Part III) describes his research for the causative agent of "spotted fever," which he has observed in a considerable epidemic in Tsingtau, in the spring of 1911. Most of the cases occurred in Chinese coolies, but a considerable number of Europeans were also attacked, with a death rate considerably higher than in the case of the former. In 38 per cent. of the cases observed, a diplococcoid bacillus was found in the blood or the organs, which there is reason for supposing the causative agent. It is prone to exhibit marked variations when grown upon different media, in some of which, indeed, it appears as if it were a member of the streptococcus group, although its staining with Gram, its growth in milk and its morphological appearance are against this. Late in the disease, preferably four to two days before the fall of the fever, the blood culture is most likely to succeed, and at this time even smears of the blood may be successful in demonstrating the organism. The agglutination test proved positive only in low dilutions and in a few cases, and inoculation of pure cultures in apes was succeeded by a short febrile period after a considerable time of incubation. Once more the question is whether we deal with the actual agent or with a secondary infection frequently present.

The Disinfectant Power of Alcohol.—BEYER (*Zeit. f. Hyg. u. Infekt.*, 1911, Band lxx, Heft 2) details a most painstaking study of the effect of alcohol in various dilutions in killing pathogenic and pyogenic organisms. Seventy per cent. (by weight) alcohol far excels all other solutions in bactericidal power, being 30 times as effective as 60 per cent., and 40 times as effective as 80 per cent. alcohol. Beyer states that solutions under 60 and over 80 per cent. are useless for disinfection for practical purposes. Alcoholic solutions changing slightly by evaporation change greatly in their effectiveness. Absolute alcohol will not kill dried bacteria, and mixtures of alcohol with chloroform, ether, benzol, glycerin, etc., have not increased power over that possessed by the mixture with water. *Eau de cologne* is stronger bactericidally than the same strength of watery solution. Etheral oils alone or in alcoholic solution are not practically useful, and carbolic acid, lysol, and kresol do not gain by solution in alcohol. Iodine in alcohol surpasses all solutions in power, and kills anthrax spores in one minute; even iodine in one-quarter per cent. solution is effective as a practical disinfectant. Decolorized iodine is weaker than colored, but is still very potent. Chlorometacresol and "eusapyl" gave excellent results as hand disinfectants, the alcoholic solution of the former ranking next to the tincture of iodine in its efficiency.

Appendicitis Caused by Parasites.—It will be necessary for most writers to revise their ideas upon this subject, if much more evidence be adduced similar to that brought forward by R. L. CECIL and K. BULKLEY (*Jour. Exp. Med.*, March 1, 1912, xv, No. 3). Many will recall that Metchnikoff has for years pleaded the cause of the vermiform parasite in causing appendicitis, without making many converts. Cecil and Bulkley examined 148 appendicees from children aged between two and fifteen years. Nineteen were normal, removed at autopsy, and of these 3 showed oxyuris; 129 were operative cases, and 19 of them showed parasites, 17 times oxyuris, and twice trichocephalus. In 15 out of the 19 cases, the parasites were associated with non-suppurative appendicitis, in 4 cases with a gangrenous form of the disease. The changes observed in the former (catarrhal) cases were confessedly slight, and Cecil and Bulkley state that in 70 per cent. of the 19 cases there were mucosal lesions unquestionably produced by the parasite. The oxyuris, they think, burrows into the lymph follicles causing extravasation of blood into the surrounding tissue, and often out through the mucosa. Hemorrhagic ulcers at times are seen; but it is stated that a characteristic feature of the oxyuris lesion is the absence of inflammatory reaction, which seems surely to be a strong piece of evidence against the authors' contentions in the matter. The trichocephalus tends to burrow beneath the epithelium. The conclusion which Cecil and Bulkley draw is that oxyuris and trichocephalus, when they occur in a diseased appendix, are, in most cases, the exciting cause of the pathological changes found. We may add that it seems almost necessary to know what is the state of the bowel in general with regard to parasites, before accepting fully the conclusions, for our own experience at the autopsy table indicates that most cases of parasites in the alimentary tract are in foreigners, that some of these are intensely infested with them; appendicitis in such cases would be

more likely to be accompanied by parasites than appendicitis in the native-born, common though oxyuris is in children of all nationalities. New York hospitals, too, are very certain to show, even among children, a good many foreign born. Some very beautiful photographs are shown of the parasites in the appendical tissue.

The Production of Antibodies by Artificially Grown Tissues.—It has been stated that "it is those cells in the body which anchor the toxins which produce the antitoxins," or otherwise, that the cell which is liable to attack is the one which forms the defense. A beautiful confirmation of this comes from A. CARREL and R. INGEBRIGHTSEN (*Jour. Exp. Med.*, March 1, 1912, xv, No. 3), who placed antigen with tissues which were cultivating artificially, and found that the newborn cells in the culture produced antibodies. Guinea-pig bone-marrow and lymph nodes were grown in guinea-pig plasma, and goat blood was used as antigen. Only cases whose technique was perfect, are reported, and it was found that the fluid of the cultures containing goat blood acquired a hemolytic power upon goat corpuscles, while the serum of control cultures remained negative in this regard. This hemolytic power was preceded by phagocytosis of the goat corpuscles by the guinea-pig leukocytes; no phagocytosis was seen in the first two days, but on the third day of incubation of the cultures phagocytosis was well marked. Hemolysis occurred without the addition of complement, by substances acting as natural hemolysins.

Means of Immunity in Bubonic Plague.—SIGNORELLI (*Lo Sperimentale*, February, 1912, Anno lxxv, fasc. V-VI) details the trend of opinion voiced at the international conference at Mukden regarding means of vaccination and therapy in the bubonic plague. It is considered that while it is perfectly proved that vaccination is an efficacious means of defence against the bubonic form of the disease, it cannot be said that it is effective in the case of the pulmonary form of the disease. The best method, and the one most widely used, is that of the inoculation of dead bacilli (Haffkine), while the method of Lustig and Galeotti, of using the nucleoproteins of the bacilli, is also useful. Indeed, the production of antibodies agglutinative to the bacilli has been repeatedly confirmed, and is best furthered by the use, as antigen, of the nucleoprotein of the bacilli prepared according to the method of the last named experimenters. Serotherapy, it must be admitted, has proved quite ineffectual in the treatment of the pulmonary form of the disease; the most that could be claimed was a prolongation of the course of the disease, and this only after the use of large quantities of serum.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

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THE
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JUNE, 1912

ORIGINAL ARTICLES

SURGERY OF THE BILE DUCTS.¹

BY JOHN B. DEAVER, M.D., LL.D.,

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It can truly be said that our present knowledge of the pathology of the abdominal viscera, and particularly of those of the upper abdomen, is directly due to the development of modern abdominal surgery. And foremost among these structures whose diseased conditions have been made manifest by surgery we can consider the biliary system with its accessory organs, the gall-bladder and the bile ducts, and the pancreas.

I have dwelt many times upon the importance of living pathology, the direct examination of diseased processes *in vivo*, the opportunity for which has caused it to be truly said that the internist walks by faith, the surgeon by sight. The study of living pathology enables the surgeon, and the internist if he will avail himself of its opportunities, to distinguish fundamental conditions from end results. It enables us to attack pathological conditions in their incipency and often to diagnosticate them at a time when treatment will still be of avail.

Surgery of the bile ducts, in association with the work of men in the laboratory, has demonstrated that with the exception of malignant disease all the conditions which call for surgical interference upon any part of the biliary tract have their origin in infection. Even malignant disease, though probably not itself of infectious origin, seems to bear some relation to antecedent infec-

¹ Read before the Medical Society of the State of New York, Albany, N. Y., April 17, 1912.
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tious processes since it is found most often in organs which bear the traces of previous inflammation. The long train of biliary disease, with its complications and sequelæ, has therefore as its one exciting factor the harmful activity of pathogenic micro-organisms.

The infecting agent may reach the biliary tract in a number of ways, but it seems likely that it generally arrives by way of the portal circulation. There is no doubt, however, that microorganisms may enter the biliary tract directly from the duodenum, and this seems to be the case in those instances of cholecystitis and cholangitis directly consequent upon an intestinal catarrh.

Whatever the route of infection a number of organisms are concerned in the production of biliary disease, each one of which alone or in combination with others gives rise to many different pathological conditions.

As a general rule it may be accepted as proved that low grade infections by microorganisms greatly attenuated give rise to gall-stone disease, or cholecystic inflammation with the formation of stones, while acute invasions of the biliary tract by organisms of high virulence give rise to acute forms of cholecystitis, cholangitis, and their accompaniments too rapidly to permit of the formation of stones. Such acute infection again may partially subside and be converted into a sluggish stone-forming catarrh.

As has been mentioned, no one form of disease of the biliary tract can be identified with a particular organism. Thus, of 142 operations in 1911 on the biliary tract for various lesions, 34 showed bacillus coli, 50 showed no growth, in 46 the organism was not mentioned, 2 showed *Bacillus typhosus*, 7 *Staphylococcus albus*, 1 streptococcus, 1 *Bacillus pyocyaneus*, 1 *Bacillus aërogenes*. It is worthy of note that in many instances where infection was evident, that is, in the presence even of pus, cultures showed no growth. Either the organisms present were not such as could survive upon ordinary culture media, or that which seems more likely, the offending bacterium had died out while the products of its activity remained.

The preponderance of the colon bacillus is not remarkable. It is a well-known fact that this organism is at all times present in a large portion of the alimentary tract and that most infections of a portion of this tract soon become mixed in the presence of this widely distributed and hardy organism. The colon bacillus then overgrows the original invader and alone is found when the case comes to operation. This fact together with the ease with which this organism is cultivated and identified probably gives it a statistical importance somewhat beyond its actual deserts. There can be no doubt, however, that the colon bacillus may be the infecting organism at the outset and by itself may produce all the varied consequences of infection of the biliary system.

In other series the *Bacillus typhosus* has been found in a greater percentage of cases. Thus in 182 cases of cholelithiasis, reported by me in 1906, there were cultures made in 94, and of these, 13, or one-seventh, showed the presence of the typhoid bacillus. In one instance this organism persisted forty-one years after the original infection. We have found this organism in the gall-bladder in cases where the most careful inquiry failed to elicit anything like a previous attack of typhoid fever. I have known typhoid fever to immediately follow an operation for the removal of stone from the gall-bladder where cultures from both the gall-bladder and the interior of the stone removed showed the typhoid bacillus.

These figures are of interest in view of the possible role of the *Bacillus typhosus* in the causation of cholelithiasis. It has been found that a large proportion (in this series 22 per cent.) of gall-stone cases give a history of having had typhoid fever, and it seems in many of these as if we could directly trace the beginning of symptoms referable to the biliary system to a period not long after the typhoid infection. The typhoid bacillus has repeatedly been demonstrated in the centre of biliary calculi, and it is probable that it bears a closer relation to the origin of biliary disease than the study of cultures at the time of operation would indicate.

Each organism of the small series given, and others also, has been found capable of giving rise to the most diverse conditions within the biliary tract, and no special set of changes can be charged to any particular organism.

In contradistinction to the old view that most cases of gallstones are without symptoms, we know now that all of them have symptoms and most of them very evident ones. We have learned that infectious conditions giving rise to marked pathological changes in the right upper quadrant of the abdomen are not different from similar processes in any part of the body, and that they must and do make themselves known by symptoms needing only correct interpretation to make a diagnosis certain. As our diagnostic powers improve and surgical cure is more often sought, we shall meet with fewer and fewer instances of the extensive complications found in so many cases of this series, just as it is rare nowadays to find an instance of the huge ovarian cysts formerly so common and so spectacular from the operative standpoint.

Since infection is the underlying cause of biliary disease we must rely in this, as in other cases of infective disorders, upon that great surgical principle of the treatment of infection—drainage. And we have demonstrated that the biliary tract is no exception in yielding to the correct application of this principle. Every operation upon the biliary ducts must serve a double purpose, it must meet the immediate mechanical demands of the conditions found, and it must furnish drainage for a sufficient length of time to cure infection.

Could we get these patients in the early stages of the disease there would be nothing to meet but the infection—in other words, cholecystostomy would suffice; a simple operation quickly performed, and, with proper care in the selection of patients, almost without mortality. It is a high aim to get our cases in this stage, but it is not too high, and should command the united efforts of the profession. Unfortunately it is in just this stage that the disease is most difficult of diagnosis, the physician most reluctant to advise, and the patient to accept operation. The same educational campaign which has won such a signal victory in appendicitis must now be carried on in this field. All cases of indigestion should be most carefully scrutinized for the evidence of localization in the gall-bladder. Slight epigastric distress; occasional tenderness in the right hypochondrium, sometimes accompanied by a slight rigor; a catch in this region during inspiration; excessive flatulence and belching; “bilious attacks,” and at intervals perhaps a faint icteroid tinge in the skin without definite jaundice; a perceptible increase in the tension of the upper right rectus muscle as compared with its fellow; indigestion, so-called, not definitely associated with the taking of food (in my series 64.7 per cent. had “indigestion” of varying degrees either before suffering from acute attacks or in the interval), all these are highly significant of beginning disease of the bile passages. I will grant that such symptoms do not at once call for operation, but they call for most careful supervision, and not the casual notice with which the profession has to its disgrace hitherto treated them, until the laity have come to disregard such symptoms and often fail to seek the advice by which many cases could be aborted.

This is the field for medical therapy, for Carlsbad treatment if the patient can afford it, not those later complicating conditions, the treatment of which by the physician is no more promising or rational than is that of the quack who either dissolves the stones or evacuates them in the form of soap-balls after huge doses of oil.

The time of election for operation is when medical treatment fails to control the inaugural symptoms previously mentioned or when they recur after supposed cure. Failing this, we have introduced into the situation an almost innumerable variety of factors dangerous to the patient's health and life, and for the surgeon a source of difficulty, of mental anxiety, and disaster to his ambition for enticing statistics. The most common result of infection is gallstones. The mild cases of infection are more dangerous in this respect than are the acute infections, for it is the low-grade catarrhal inflammation which causes desquamation of the lining epithelium, the production and deposit of cholesterin and biliary salts which result in stone formation, while more virulent processes do not at once cause stones, though they do give rise to other and perhaps more dangerous conditions. Later, when the

process becomes subacute or chronic, stones may be found, though not invariably. So long as the calculi remain in the gall-bladder the conditions are still practically ideal for operation. It is their further wanderings into the cystic, common, or hepatic ducts that give trouble alike to surgeon and patient.

The next complicating factor in order of frequency is adhesions. In this series they were present in about one-half the cases (45.4 per cent.). They are the result of pericholecystic or periduodenal inflammation. They are conservative so far as life is concerned, but they are often destructive to function. As I stated some years ago, "In many cases the symptoms and gravity of gall-bladder lesions are due not to the gall-bladder affection *per se*, but to the accompanying adhesions."

I believe that pericholecystic adhesions the result of gall-bladder and duct infection often give a clinical picture which is identical with that found in gallstone disease, and do so in the entire absence of gallstones at any time, and after operation they are capable of causing symptoms which mimic gallstone colic. In one case in this series the duodenum was constricted almost to the point of absolute obstruction by a band emanating from a previous infection of the gall-bladder, and in another the outer portion of the wall of the duodenum was invaginated and adherent. Aside from certain congenital abnormalities of the peritoneal attachment, adhesions in the abdomen are always the result of inflammation, and they may give rise to the most baffling but distressing symptoms. Abdominal adhesions are very unsatisfactory material for surgical treatment, since they are apt to reform after operation, and it is largely a matter of chance whether their new situation will be any more favorable for the patient. Hence the importance of eliminating by early operation this source of dissatisfaction with operative results.

It is impossible in a short paper to treat fully of the various clinical results of these processes. Ulceration, infiltration, perforation, gangrene, cicatricial contraction, and stenosis all are common, and affect in various degrees the different portions of the gall-bladder and ducts. In one case I observed a spontaneous cholecystogastrostomy in the process of making, a stone being still lodged in the opening from the gall-bladder to the stomach. In another case stones were embedded in the stomach wall, which had not been perforated. In still another instance the patient came with a sinus in the right side of the abdomen, which had discharged gallstones, Nature thus having effected what the surgeon could have done before with far greater safety to the patient. To permit such conditions as this to arise may be called conservative treatment, though just what it conserves is a mystery. In this field if not in politics we should all be progressives.

Last and not least we may have as a result of gall-bladder infec-

tions, or as a result of the same infection attacking the pancreatic tract, a pancreatitis, acute or chronic. Acute pancreatitis demands consideration as a separate clinical entity. But chronic pancreatitis is so often found coexistent with biliary infection that it may truly be considered as a part of the clinical picture of biliary infection. It is unlikely that pancreatic lesions are the result of direct extension of infection up the pancreatic ducts. Far more important it has seemed to me, is the extension by way of the lymphatics. The hardening of the head of the pancreas so often noted during operations on the biliary tract is due in its earliest stages at least to lymphatic infection and congestion, and is possible of relief by drainage. Our views concerning the nature of these swellings of the pancreas and their origin have been set forth in an article by myself and my assistant, Dr. Pfeiffer, in the *AMER. JOUR. MED. SCI.*, 1912, cxliii, 4, 473. How important is the early relief of this condition must at once be evident. To restore a chronically diseased pancreas to normal after the deposit of dense fibrous tissue is impossible by any means now at our command. Most if not all of these instances of pancreatic change which have been so wonderfully benefitted by operative procedures must have belonged properly in the category of pancreatic lymphangitis, and were not, properly speaking, cases of chronic pancreatitis.

But, nevertheless, it seems likely that such a pancreatic lymphangitis is the forerunner of a true chronic pancreatitis and if we are able to cure the underlying condition we may be said to cure the final one by preventing it. In this sense I believe that diabetes is at times a surgical condition. While the pancreatitis induced by infections of the type under discussion does not often destroy sufficient of the islands of Langerhans to cause diabetes, there is sufficient clinical and pathological evidence that it may do so, and thus a timely operation may be the means of avoiding this dangerous condition. I have on more than one occasion seen glycosuria clear up after a successful drainage of the infected biliary and pancreatic ducts.

It is evident then that by timely operative procedures upon the biliary passages we are able to do far more than simply to remove a few gallstones or loosen a few adhesions. We are able to apply the principle of drainage to infections here as in other parts of the body, to cure first causes, to do away with the harmful results of invasion by pathological bacteria.

Aside from traumatic and neoplastic affections of the biliary ducts the conditions calling for surgery may be grouped as follows: (1) Non-calculous cholecystitis, (2) calculous cholecystitis and its complications, (3) pancreatic disease.

In non-calculous cholecystitis there is but one problem—to remove the results of inflammation and to insure sufficient drainage for a proper length of time. The gall-bladder may require

removal if gangrenous or inordinately thick and functionless, though I attempt to preserve it in all cases.

Pancreatic disease furnishes a strong indication for temporary or permanent drainage of the biliary tract, temporary by direct tube drainage or permanent by some form of anastomosis between the biliary system and the alimentary canal to give greater drainage than the natural outlet affords. In my practice this has generally consisted of cholecystoduodenostomy.

Of the methods of treatment of pancreatic conditions found at operation I shall speak more at length later.

Kocher's oft-quoted remark that "Gallstones belong neither to the surgeon nor to the physician, they belong to the patient," is quite correct. It is, indeed, the patient's privilege to have his bodily ailments treated in such manner as he sees fit. Yet were every gallstone patient informed of the possible results of his condition, and shown the difference between the mortality and end results in early and late operations, there is but little doubt in my mind that he would quickly turn to surgery for relief.

What, then, are the indications for operation in diseases of the biliary ducts and gall-bladder? (1) More than one attack of true biliary colic; (2) symptoms suggestive of upper abdominal adhesions and chronic biliary insufficiency; (3) hydrops of the gall-bladder; (4) obstruction of the common duct; (5) the occurrence of acute infections complicating previously existing biliary disease; (6) the evidences of pancreatic disease, acute, subacute, or chronic.

No physician or surgeon of the modern school expects to see more than a fraction of his gallstone patients come to him with a history of biliary colic. Numbers, indeed, give a fair approach to a classical history of gallstones, but the majority give a far vaguer combination of symptoms often with, but at times without, any history of jaundice.

In comparison with the total number of cases suffering from gallstones or their effects, classical cases are few. I sometimes think that the simple rule "fair, fat, and forty, and belches gas," would be a safer maxim for our students if we wish them to recognize gall-bladder disease than is the hard and fast clear-cut picture so faithfully embalmed in most of our text-books.

Just a word about the age at which the gall-bladder is likely to be infected. We have been taught that it is a disease of the later years. The average age of the 142 patients was 40.8 years. The average duration of symptoms was 6.6 years. On the average, then, these patients were but thirty-four years of age when known to be infected. In other words, the beginning of the condition is in early adult life, and the reason why it has been considered a disease of the declining years is because the early symptoms go unrecognized until the accumulation of pathology forces a diagnosis and treatment. Six and one-half years is too long for the

physician to ponder over a case that is trending toward operation as the only means of relief. An interesting feature of cholelithiasis is the liability to recrudescence after labor. In the present series there are 3 instances of gallstone colic following immediately after parturition. All had had symptoms of gall-bladder disease previous to the last pregnancy. These attacks were the most severe that the patients had experienced.

Pain that could be called biliary colic was present in 80 per cent. of the cases; jaundice in 47 per cent. These percentages are high in any operative series, since they are striking, severe, and of an order to induce the patient to seek operative relief. Bearing this in mind it is apparent how relatively infrequent a symptom of gallstones these vaunted symptoms really are. A low incidence of these symptoms in the operative figures of a surgeon is a tribute to the intelligence of the profession among whom he labors.

The second group of these cases in which I consider operation indicated, that is, those with symptoms of upper abdominal adhesions and chronic biliary insufficiency, is a large one. It includes many gallstone cases and others of non-calculous cholecystitis and cholangitis which in former years would have been called symptomless because of the absence of pathognomonic signs. And although we find in these patients no such absolute indication for operation as the occurrence of biliary colic, yet I maintain that a carefully taken history will localize the trouble in the biliary tract and that the surest cure is drainage.

Hydrops of the gall-bladder and obstruction of the common duct give symptoms which are quite definite and well known, and it is necessary only to mention these conditions to make our statement of operative indications complete. It must not be forgotten that one or more stones may be present in the common duct without causing jaundice, and it has been my experience to find this condition in 3 out of 32 cases operated upon in the University Hospital in the last year and a half. Needless to say this is the most favorable time for operation upon stone in the common duct.

In common duct obstruction I prefer to operate in the interval between attacks of complete occlusion. What surgeon does not prefer to have his patient in the best possible condition for operation? I take issue, however, with those surgeons who, seeing a patient during acute obstruction, decide to wait until the obstruction has been relieved before operating. This may be good for the surgeon's results, since he is relieved of the necessity of operating upon certain of the more severe cases who will seek operation elsewhere when the condition instead of improving becomes worse.

I do not, of course, advocate operation in every case of acute obstruction of the common duct during the attack of colic nor during the few days immediately following, but I do not always wait for the subsidence of jaundice, for at times this does not occur

until the patient is emaciated and weakened in the extreme, to say nothing of the adhesions, etc., generated by the infection. The time to be of most service to a patient with obstruction of the common duct is during the existence of the obstruction when by operation we may come to the rescue of the liver and inflamed bile passages. After the first few days there is no greater danger of causing infection of the peritoneum than subsequently. Hemorrhage, one of the greatest dangers, does not occur in the early stages but only in the cases where a cholemic state has existed for a long time. In all cases where I fear hemorrhage I fortify the patient with injections of blood serum preferably obtained from a healthy member of the family. Large doses should be used—from 50 to 200 c.c. given subcutaneously. I believe serum is of value in this connection. Human serum is preferable to that of the horse or other animals, for obvious biological reasons. Gelatin is useless for the prevention of capillary oozing, and the salts of calcium, while they may effect a reduction in the coagulation time of the blood, do not appear to have much influence upon cholemic hemorrhage.

The evidence of pancreatic disease points also directly to the need for operation. Unfortunately it is most difficult to be sure of this condition. Chronic pancreatitis, so often associated with disease of the biliary tract, only occasionally gives rise to symptoms which could not just as well be accounted for by gallstones or chronic non-calculous cholecystitis.

When, however, the character of the stools, with an intermittent diarrhea and constipation, and those grave metabolic changes attributable to pancreatitis, give evidence of pancreatic disease, I consider operation indicated even in the entire absence of symptoms pointing to disease of the biliary tract. Particularly is this true when to the symptoms mentioned we have added a glycosuria. In the present series the pancreas showed recognizable lesions chiefly of the nature of pancreatic lymphangitis in 45 cases (32 per cent.). In 3 of these there were some flecks of fat necrosis in the vicinity revealing the presence of an acute exacerbation of the chronic inflammation.

I have had the Cammidge "C" reaction performed in 84 cases of the present series, with the following results: Pancreas involved—Cammidge positive, 9 cases, Cammidge negative, 20 cases. Pancreas uninvolved—Cammidge positive, 8 cases, Cammidge negative, 48 cases.

This is a poor showing for a pathognomonic reaction, and I can therefore place no dependence in it, as these results substantially correspond with about 400 previously obtained in the laboratory of the German Hospital in these and other conditions.

Operation must accomplish three things: (1) It must meet the actual pathological condition and relieve it; (2) it must remedy

if possible the underlying cause; (3) it must if possible prevent a recurrence of the conditions found by rendering the return of the cause unlikely.

The actual pathological conditions met with in surgery of the bile ducts consist of three great groups: (a) Infection; (b) calculi; (c) of adhesions about and malformation of the gall-bladder and ducts as a result of infection.

Gallstones when found are to be removed, of course, it matters not in what part of any duct they may be, and it is, as a rule, possible to do this if the operator be competent and patient. Their removal from the gall-bladder and cysticus is generally a matter of small difficulty, unless the stones are very small and buried within the mucosa of the gall-bladder or in a diverticulum.

The removal of a stone from the choledochus is often a matter of great difficulty, particularly if it be situated in the pancreatic or the intraparietal portion of the duct. When the stone is in the first portion of the common duct, or can be pushed into it, the method of removal consists in direct incision of the duct over the stone and its removal. When the stone is in the second or third portion of the duct an effort should be made gently to bring it up into the more accessible supraduodenal portion of the duct, or failing in this, to dislodge it into the duodenum. Retroduodenal and transduodenal methods of approaching a stone in the common duct are distinctly more dangerous than simple choledochostomy, and only very rarely necessary. At times a soft stone which is lodged in the lower extremity of the duct may be broken up and removed piecemeal with the gallstone scoop. I am never satisfied until I can pass the olive pointed end of a good sized gallstone explorer through the papilla of Vater into the duodenum. Stones which have worked their way upward into the hepatic ducts are very difficult and at times impossible of extraction. These are one cause of the recurrence of symptoms after the removal of common duct calculi, and is a possibility that we cannot control. As a rule the downward flow of bile keeps the stones in the lower duct where they can be removed.

A point of some importance in connection with surgery of the common bile duct is a variation from the normal in the formation of the choledochus in which the cysticus and hepaticus join near the duodenum, and the hepatic duct entering posteriorly appears much as a branch of the cystic duct, the latter seemingly being continued directly into the common duct.

In addition to the removal of gallstones in calculous cases we must make certain that embarrassing pericholecystic adhesions are freed. It is not always advisable to release all the adhesions when the lesion can be satisfactorily dealt with without doing so. The continuity of the bile passages must be established or provision made for the proper discharge of the bile.

The removal of adhesions and attention to the state of the biliary ducts constitute also the main features in surgery of the actual pathology of non-calculous cholecystitis, which presents in every way the problems of gallstone disease minus only the actual presence of the stones.

The remedying of the underlying cause of disease of the biliary system, when not malignant, depends upon our ability to combat infection in this field. Since infection is the direct causative factor in all the lesions with which we have to deal, it is only when we successfully meet it that we can be certain that everything possible has been done for the relief of the patient.

And, as in infection in any other part of the body, our reliance must be upon drainage, this must be our watchword particularly in biliary surgery, for since infections here are so persistent in their course and insidious in their harmful action, it is essential that nothing be left undone for their final cure.

I believe, therefore, that in every operation upon the gall-bladder it should be drained, granting that the viscus is not diseased to the extent of being rendered functionless.

Drainage of the common duct is imperative when we have opened it for stone, in all grades of cholangitis and particularly after cholecystectomy in the presence of liver infection and pancreatic involvement, even when there are no stones in the duct. H. Kehr² recommends that the choledochus be drained after cholecystectomy when there is: (1) Thickening of the pancreas, especially of the head; (2) when the choledochus is thickened and distended; (3) with a history of icterus, chills, and passing of stones; (4) when a considerable amount of the cystic duct is left and it is split to the common duct; (5) when many small stones are found in the common duct; (6) drainage of the hepaticus when cloudy pus oozes from the stump of the cystic duct, proving infection of the choledochus; (7) in the presence of liver enlargement, indurated liver, and cirrhosis.

With these indications for common duct drainage after cholecystectomy I fully agree.

All cases of infection of the biliary passages, unless very transient or coming as intercurrent affections in acute illness, demand drainage of the gall-bladder. Of these any that show marked infection or a cholangitis demand common duct drainage also.

For stone in the gall-bladder I consider cholecystostomy the best operation. It has a slightly lower mortality, is followed by fewer adhesions than cholecystectomy, and leaves the gall-bladder as a possible future drainage outlet in case of serious biliary or pancreatic disease. Excision of the gall-bladder I practise in cases of: (1) Malignancy; (2) hydrops of the gall-bladder; (3) chronic empyema of the gall-bladder; (4) gangrene; (5) when the cystic

² Arch. f. klin. Chir., 1912, v. 97, 2, p. 301.

duct is not patulous; (6) when many small calculi are imbedded in the gall-bladder mucosa.

When in the course of an operation upon the biliary tract we find a pancreatic lymphangitis or a beginning pancreatitis drainage is invariably indicated. If the gall-bladder is greatly diseased and full recovery doubtful in a case complicated by pancreatic lymphangitis, I consider it an indication for cholecystectomy. Drainage of the common duct should then be established. There is no doubt that the pancreas may be drained through the opening in the common duct, as I have noted the peculiar irritating character of the discharge in certain of these cases. In an instance seen within the last month the patient's skin was severely excoriated by contact with the discharge from the common duct, and the presence of pancreatic ferment was proved by the digestion of blood serum and starch in alkaline solution. In this case I had passed a good-sized gallstone explorer through the ampulla of Vater and had no doubt of its patency. When the pancreatic duct does not open into the sinus of Vater, of course this avenue of drainage of the pancreatic secretion is not possible; but the operation is still productive of good in that the primary focus of infection in the gall-bladder is abolished.

If the lesion be primarily of the biliary ducts, common duct drainage will be sufficient, though temporary, to meet the indications furnished by the pancreatic condition.

If the pancreatic condition be the main one or is the one causing symptoms, permanent drainage by a cholecystoduodenostomy is indicated, and it has been a procedure most brilliantly effective.

The surgery of the biliary tract has been made satisfactory from the standpoint of operative mortality and end results.

In conclusion let me again urge the danger of procrastination and too much deliberation. It is well known that he who deliberates is lost, but under these circumstances it may be the unhappy lot of the patient to be numbered among the lost. It should be mortifying to the physician to see the disastrous results of infection laid bare, to say nothing about the mortification of the patient. The full story of the autopsy *in vivo* has not yet been told. The new pathology is now being written.

The dawdling with duodenal buckets, fallacious laboratory methods, etc., I deplore; and could patients be educated to their uselessness, they, too, would despair. The resources of surgery are rarely successful when practised upon the dying, nor are they so uniformly successful when pathology is advanced as when it is in its incipency.

At least nine-tenths of the mortality of operation so-called is in reality the mortality of delay. Bearing this in mind, we must place the problem of the reduction of invalidism and death due to biliary infections in the hands of him who sees the patient first, namely, the family physician.

A CRITICAL STUDY OF OXYURIS AND TRICHOCEPHALUS APPENDICITIS.

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In previous reports we have attempted to draw a brief clinical picture of oxyuris and trichoecephalus appendicitis and to demonstrate the pathology of the disease. In the present paper we wish to review the literature of the subject and to attempt by an analysis of it and of our own cases to identify parasitic appendicitis as a separate disease having an etiology, pathology, and symptomatology of its own. We are considering only *Oxyuris vermicularis* and *Trichoecephalus trichiura* in relation to appendicitis, because they have been the two parasites most frequently associated with this disease and because the lesions and symptoms which they produce are, in a general way, similar. In the following pages we will not attempt to separate the oxyuris from the trichoecephalus cases except in the section on pathology.

INCIDENCE. The first reports which we can find of clinical cases of appendicitis in which the removed appendix contained oxyuris or trichoecephalus were published in 1900 by Beyea,⁶ Frazier,²¹ and Guinard,²⁶ the first two writers reporting oxyuris, and the last trichoecephalus. Still,⁵⁴ however, in 1899 described oxyuris in the appendices of children at autopsy. Shortly after this, in 1901, Metchnikoff⁴¹ reported 3 cases of appendicitis due to *Asearis lumbricoides*. It was this paper which served to awaken interest in parasitic appendicitis, for it was immediately followed by a series of articles, some mere case reports, others discussing more or less fully various phases of the subject. It is interesting to note the incidence in various countries of oxyuris and trichoecephalus in the feces, in the intestinal tract and appendix at autopsy, and in resected appendices. In France the figures vary. Brumpt and Lecene⁸ (Paris) state that in 10 per cent. of the appendices of adults coming to autopsy either oxyuris or trichoecephalus are found. A year later Brumpt⁷ (Paris) reports finding oxyuris in the appendix in 3.5 per cent. of 800 autopsies. In 13 autopsies on children he found oxyuris in the appendix twice (15 per cent.). In the surgical clinic of August Broca oxyuris was present in the appendix in 24 out of 60 cases of appendicitis operated on, or 40 per cent. Railliet⁴⁹ (Paris) examined 119 resected appendices and found oxyuris in 48.74 per cent. In one case trichoecephalus was also

present. Oelnitz,⁴⁵ at Nantes, observed 21 cases of appendicitis, in 18 of which trichocephalus eggs were found in the stools. Martin⁴⁰ says that in Montpellier oxyuris was found only once in 500 resected appendices, and then quotes a personal communication from Vedel, who states that, in 1900-1901, 50 per cent. of the cases of appendicitis at Montpellier had trichocephalus in their stools. In Germany Hoepff³² reports finding oxyuris in 24 out of 117 resected appendices, or 21 per cent. Delsmitt¹⁷ examined the feces of 21 children who had appendicitis, and in 18 of them found eggs of either trichocephalus or ascaris. Oppe⁴⁶ reports finding oxyuris in 5 out of 60 resected appendices, or 8.3 per cent. Still⁵⁴ (London) in 200 autopsies on children under twelve years of age, found thread-worms in the intestines in 19 per cent. of the cases; in children between two and twelve years of age, 32 per cent.; in 6 cases they were found only in the appendix. Matigum during four and a half years in China, where intestinal parasites are very common, saw only 1 case of appendicitis, and that appendix showed no worms. Treille⁵⁶ reports similar findings in Algiers.

In the United States the subject seems to have been largely overlooked. Crile¹³ summarized "1000 cases of appendicitis with observations on etiology," and fails to mention worms of any sort. Deaver¹⁶ found oxyuris once in 500 appendectomies on children. Hanley²⁹ reports finding at operation an appendix filled with pin-worms, and says it is the first he has seen in 500 appendectomies. Kelly²⁶ examined 460 cases of appendicitis, with special reference to pathogenesis, but fails to enumerate worms as a possible etiological factor. Erdman¹⁹ found pin-worms in 4 out of 250 children's resected appendices. In New York, Schloss⁵³ examined the stools of 280 consecutive children and found that 11.07 per cent. carried trichocephalus and 8.21 per cent. oxyuris. It is interesting to note that in 3 of these cases (all oxyuris) the patients complained of abdominal pain, 2 of them localizing it on the right side.

Our material has been obtained largely from the two surgical services of the Presbyterian Hospital, a small part of it coming from other hospitals in New York, and one appendix from a neighboring town. The material consists of 148 unselected appendices of children aged between two and fifteen years, 129 being clinical and 19 of them autopsy cases. We have also studied 4 adult appendices infested with oxyuris.

Of the 129 clinical cases, 19 of them, or 15 per cent., contained either oxyuris or trichocephalus; 89 appendices of the series were gangrenous or suppurative in type. In these we found parasites only 4 times, or in a fraction more than 4 per cent. In the non-suppurative cases parasites were found 15 times, or in about 38 per cent. While we have made no attempt to determine the incidence of the disease in adults, we have encountered 4 adult cases, and these we include in our report. In 19 appendices obtained

at autopsy upon children aged between two and fifteen years, we have found worms in 3, or about 15 per cent. We believe, however, that if the autopsy series could have been as large as the series of clinical cases, the incidence of parasites in the normal appendices of children would be much smaller than 15 per cent.

We have been able to collect from the literature 49 definite case reports of appendicitis associated with oxyuris or trichocephalus. To this list we have added 23 of our own cases, making a total of 72 reported cases. In the table we have given a brief outline of each case. In 61 of these the age is stated. Fig. 1 shows graphically the large proportion of cases in young people. A little over 50 per cent. occurred between the ages of six and fifteen years. The youngest case in our own series was a boy, aged three years, and our oldest case, a woman, aged fifty-four years. Kornbluh³⁸ has recently reported a case in a child, aged twenty-one months.

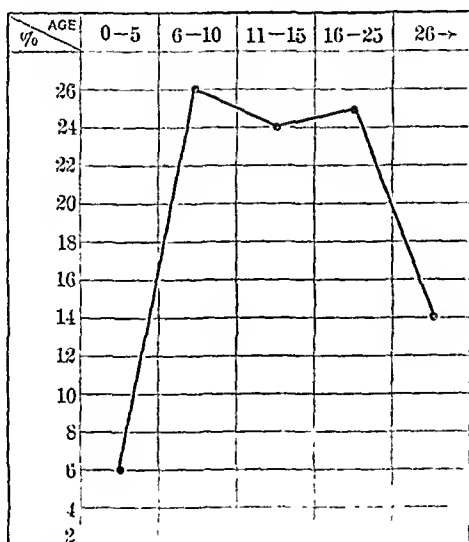


FIG. 1.—Showing the relation of age to incidence in 61 reported cases of oxyuris and trichocephalus appendicitis.

In 68 cases the sex has been stated. There were 23 males and 45 females, or about 2 females to each male.

The disease occurs in both city and country, and is by no means limited to the poorer classes. The majority of our own cases have come from tenement districts, a few from the more wealthy residential sections of the city. It will be noted that according to our figures the incidence of parasites in the diseased appendix is lower in New York than it is in French and German cities. The prevalence of oxyuris and trichocephalus in France and Germany is well known. It is probable that the incidence is higher in New York and other American cities whose population is largely foreign than it is in the smaller towns and country districts whose inhabitants are for the most part native-born Americans.

CASES OF OXYURIS AND TRICHOCEPHALUS APPENDICITIS.

Case No.	Reported by	Age.	Sex.	Type of appendicitis.	Parasite.	Number of parasites.			Pain.	Vomit- ing.	Tender- ness.	Rigidity.	T.	P.	R.	Leuko- cytes.	Poly- nuclear.	Result.
						Total.	M.	F.										
1	Allen	11	F.	Catarrhal	Oxyuris	12	+	+	+	+	103.0	120	31	25,000	...	Cured.
2	Ashurst	14	F.	Acute suppurative	Oxyuris	100.6	88
3	Béguin	21	F.	Catarrhal	Oxyuris	150	+	..	+	..	N.	Cured.
4	Beyers	22	F.	Catarrhal	Oxyuris	1	+	+	..	+	100	Cured.
5	Brumpt and Lecene	10	M.	Catarrhal	Oxyuris	Many
6	Carson	19	F.	Catarrhal	Oxyuris	1	0	1	+	+	+	Absent	103.8	116	32	Cured.
7	Carson	21	F.	Catarrhal	Oxyuris	3	+	+	+	Absent	100.6	118	28	Cured.
8	Cullane	21	F.	Catarrhal	Oxyuris	18	+	+	+	+	99.0	Cured.
9	Cutler	45	F.	Catarrhal	Oxyuris	Many	+	+	to 103.0	Cured.
10	Dooley	Adult	F.	Catarrhal	Oxyuris	20	+	+	+	+	N.	Cured.
11	Frazier	2	F.	Catarrhal	Oxyuris	Many	+	+	Died.
12	Galli-Valerio	5	M.	Gangrenous	Oxyuris and trichocephalus	Many
13	Gutrod and Fairbanks	10	M.	Catarrhal	Oxyuris	+	103.0	26,000
14	Girard	8	F.	Catarrhal	Trichocephalus	2	1
15	Guinard	25	F.	Catarrhal	Trichocephalus	1
16	Guinard	21	F.	Catarrhal	Trichocephalus	+	+	..	+	..	N.	Cured.
17	Hull	21	M.	Catarrhal	Oxyuris	+	+	..	+
18	Hunley	35	F.	Catarrhal	Oxyuris	11	+	..	+
19	Isaacs	31	F.	Catarrhal	Oxyuris	11	+	..	+
20	Hippus and Lewenson	6	F.	Catarrhal	Oxyuris	80	Few	Many	+	+	N.	Died.
21	Hutbard	9	F.	Gangrenous	Oxyuris	2
22	Hutchinson	?	F.	Catarrhal	Oxyuris	+	+	..	+
23	Kubukoff	?	F.	Catarrhal	Oxyuris	4	+	..	+
24	Kelly and Hurdon	12	F.	Catarrhal	Oxyuris	+	+	..	+	20,000
25	Ledford	7	F.	?	Oxyuris	3	+	+	+	+	102.0	120	..	+	+	Cured.
26	Ledford	30	M.	Gangrenous	Oxyuris	+	+	+	..	103.0	+	+	Cured.
27	Martin	25	M.	Catarrhal	Trichocephalus	+	0	..	+	+	+	None	Cured.
28	Martin	25	M.	Catarrhal	Oxyuris	+	+	+	+	+	Cured.
29	Mayo	?	F.	?	Oxyuris	+	+	+	+	Cured.
30	Monash	23	F.	Catarrhal	Oxyuris	+	+	+	+	Cured.
31	Monash	14	F.	Catarrhal	Oxyuris	36	+	+	+	Slight	7,200	..	Cured.
32	Moore	23	M.	Catarrhal	Trichocephalus	1	+	+	+	+	Cured.
33	Morkovitch	22	M.	?	Oxyuris	12	+	+	+	+	Cured.
34	Pabaut and Du Bois	20	F.	Catarrhal	Oxyuris	+	+	+	+	Cured.
35	Perrine	29	F.	Catarrhal	Oxyuris	1	+	+	+	+	Cured.
36	Rammstadt	20	M.	Catarrhal	Oxyuris	+	+	+	+	+	Cured.
37	Romanovitch	13	F.	Catarrhal	Oxyuris	12	+	+	+	+	Cured.
38	Thursh	20	F.	Catarrhal	Oxyuris	+	+	+	+	+	Cured.
39	Vigoureaux and Collet	?	?	Acute suppurative	Trichocephalus	1	+	+	+	+	226,000	..	Cured.

PATHOLOGY.¹² 1. The *Parasite*. The oxyuris is by far the most common parasite found in the appendix. Of the reported cases, 61, or 84 per cent., contained oxyuris, 10 or 13 per cent. trichocephalus, and in 1 case both parasites were found in the same appendix. In 28 cases the sexes of the parasites have been noted. In 10 cases the male predominated, in 11 cases the female, and in 7 cases the sexes were equally represented. Railliet,⁴⁹ however, states that the female predominates in three-fifths of the cases. The number of parasites found has varied from 1 to 150, the average being about 11. Oxyurides in various stages of development have been found (Hippius and Lewinson) not only in the lumen, but also in the walls of the same appendix, and from this Still argues that the worms must have been hatched in the appendix, and that the appendix can therefore serve as a breeding place for the pin-worm. In appendices containing trichocephalus there is as a rule only one parasite found.

There has been much discussion in the literature as to whether oxyuris or trichocephalus can be the exciting cause of appendicitis, or whether they act merely as foreign bodies and so by injuring the mucosa of the appendix form a *locus minoris resistentiæ* through which bacteria may enter and do the actual harm. That oxyuris and trichocephalus can penetrate the mucous membrane has been shown in a number of recently reported cases (Brumpt and Lecene,⁸ Galli-Valerio,²² Hippius and Lewinson,³¹ Romanovitch,⁵¹ Ruffer,⁵² Unterberger,⁵⁷ Wagcner,⁶¹ Wakefield,⁶² Walther,⁶³ Weinberg,⁶⁴ Winkler⁶⁵), and we have obtained from our own cases many sections showing the parasites beneath the mucosa. Brumpt suggests that the oxyuris punctures the mucosa for blood, but Railliet states that he has never seen blood in the body of the worm, and the parasite fails to give a reaction for iron (Unterberger). Askanazy,⁴ however, obtained a positive reaction for iron in the body of the trichocephalus, and showed that it penetrated the mucosa and sucked blood from the host. The cases of Ruffer, Wagener, and Hippius and Lewinson show that the oxyuris does lay eggs beneath the mucosa, but while it may be for this object that the pin-worm sometimes burrows, this is not its sole purpose, for in many of the reported cases, and in a majority of our own cases, only the male parasite has been found beneath the mucous membrane. It is possible that the oxyuris feeds only on the blood plasma of the host, and for this reason fails to give an iron reaction.

Various opinions have been advanced by different writers in the attempt to explain why the presence of trichocephalus or oxyuris in the appendix should cause symptoms of appendicitis or produce pathological lesions in that organ. Monash⁴⁴ suggests that the worms block the lumen of the appendix and that the contractions of the muscular wall in attempting to expel them give rise to appendicular colic, or that the irritating sharp tails of the female

initiate contractions of the appendix, thus causing colic. Oppé⁴⁶ thinks that the very presence of the oxyuris in the appendix may cause a colicky attack, the pain being due to the muscular contraction of the appendix on the worm as it tries to wriggle through into the cecum. He thinks that in this way the oxyuris may cause an attack of appendicitis and yet escape into the cecum and leave behind no trace of a lesion. Hubbard³³ goes so far as to state that there is no proof that oxyuris can cause appendicitis except in its role of a foreign body. These are the simplest of the many theories which place oxyuris in the class of foreign bodies.

The majority of writers admit that the worms puncture the mucosa, but beyond this point there is much disagreement as to whether the worms *per se* can cause appendicitis or whether they merely open the way for bacterial infection. All observers are agreed that the mucosa having been injured, bacteria may enter and set up inflammatory changes, and the majority of writers agree that an oxyuris or trichocephalus may in this way act as a predisposing factor as readily as any other foreign body. Prominent among the reports in the literature which prove this point are the cases of Girard,²⁴ Weinberg, and Galli-Valerio, in all of which marked zones of inflammation were found about penetrating parasites. That an oxyuris or trichocephalus can without secondary bacterial infection render an appendix pathological or be responsible for the classic symptoms of appendicitis is not universally admitted. From a study of our own cases and those reported in the literature, however, we are convinced that they are capable of such action. Hippius and Lewinson failed to find bacteria about penetrating oxyurides, although the parasites lay deep in the submucosa in sinuses which were lined in some places with necrotic tissue and in other places with young granulation tissue. In most of our cases in which we have found the worm embedded in the mucosa we have been struck with the absence of leukocytic infiltration about the parasite, and we have sections of appendices showing oxyurides curled up in lymph follicles around which there is neither inflammation nor necrosis. In other sections there is necrosis, but no infiltration about the invading oxyurides. Appendices infested with trichocephalus also usually fail to show any infiltration of leukocytes about the invading parasite. Examination of our specimens has convinced us that there is a definite disease of the appendix caused by *Oxyuris vermicularis* or *Trichocephalus trichiura*, and that these parasites can by their own action, irrespective of bacterial invasion, set up specific and peculiar lesions in the appendix.

2. *The Lesion.* In 66 of the 72 reported cases, including our own, the general pathological type of appendicitis has been stated or can be deduced from the context. Only 10 were of the gangrenous or suppurative variety, the remaining 58, or 86 per cent., being of a

catarrhal or non-suppurative type. Of our own 23 cases, 4 were gangrenous, 3 of these containing oxyuris, and the fourth trichocephalus. In only 1 of these 4 appendices were we able to find lesions definitely attributable to parasites. Of the remaining 19 non-suppurative appendices, we were able in 12 cases, to demonstrate microscopic lesions, which we consider pathognomonic for the parasites under discussion. Of the 7 negative cases, 4 were in adults and 3 in children. Over 4000 sections of these 7 appendices were prepared and examined but no characteristic lesions could be found. We were also unable to find lesions of any sort, parasitic or inflammatory, in our 3 oxyuris appendices obtained at autopsy. These all appeared normal in every respect except for the presence of oxyurides and swelling of the germ centres of the lymph follicles.

The following description of lesions is summarized from our previous pathological report and corresponds for the most part with that given by the writers above referred to. As the lesions produced by the oxyuris and trichocephalus differ somewhat, we will describe them separately.

LESIONS CAUSED BY OXYURIS. At operation the appendix may at first sight appear normal, but is usually found moderately swollen and rigid, with a serosa which is smooth, pale, and glistening. The vessels of the serosa may be congested. On opening the appendix the lumen usually contains a considerable amount of bloody mucus, in which the parasites may or may not be immediately visible. The mucosa is usually swollen, pinkish, and velvety. There are frequently seen scattered over it small red purpuric areas or minute hemorrhagic ulcers. There is usually no evidence of suppuration. The worms at times may be seen attached to the mucous membrane, and in 2 of our cases living worms were seen under magnification to free themselves from the mucosa. The microscopic lesions found may be divided into groups, according to the degree of damage which the parasite has done.

1. In the first group we have placed those appendices which, though containing parasites, fail to show changes other than those of a mild catarrhal nature. Externally the appendix appears as above described. The mucosa is thicker than normal, but shows no hemorrhagic foci, and the worms are seen to lie, unattached, in the lumen of the appendix. Fig. 2 shows a cross-section of such an appendix filled with oxyurides. The microscopic picture is that of a catarrhal inflammation, the crypts of the mucosa being distended with mucus and the germ centres of the lymph follicles enlarged. The other coats are usually normal, although a few scattered polymorphonuclear leukocytes, eosinophiles, and lymphoid cells may sometimes be seen. In this group we have placed 6 of our cases.

2. The second group includes those cases in which the mucosa has been penetrated by the oxyuris, but where little if any tissue

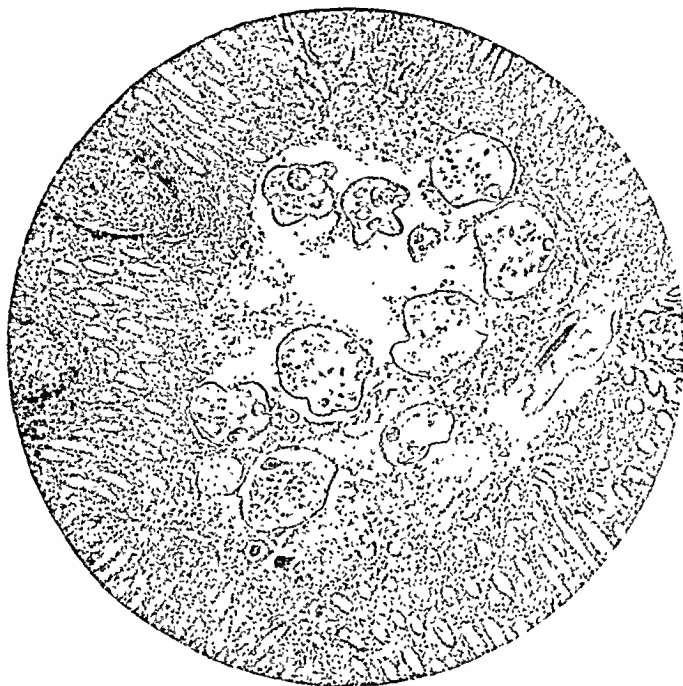


FIG. 2.—Lumen of appendix is filled with oxyurides, mostly females, whose uteri are distended with ova. Parasites separated by mucus and blood. $\times 50$.



FIG. 3.—A male oxyuris is seen invading the mucosa through a break in the columnar epithelium. $\times 107$.

has been destroyed. The parasite, usually a male, breaks through the epithelium and may or may not reach a lymph follicle. Fig. 3 shows an oxyuris invading the mucosa. Fig. 4 shows an oxyuris in a lymph follicle. Sections show the worm partially or entirely buried beneath the mucosa, or there may simply remain the empty tract from which the worm has escaped. Extensive extravasation of blood, which may be interstitial or into the appendix lumen, is present. There is no infiltration of leukocytes about the parasite or his tract. One of our cases varied from this description in showing considerable necrosis and infiltration of leukocytes about an oxyuris, but bacteria were demonstrated in the necrotic tissue. Fig. 5 shows this parasite in a lymph follicle surrounded by a zone of necrosis. We have placed 6 of our cases in this group.



FIG. 4.—Invasion of lymph follicle by a male oxyuris. No inflammatory reaction. $\times 107$.

3. The third group comprises cases showing destructive oxyuris lesions, for the most part hemorrhagic ulcers. There may be one or many of these ulcers in an appendix. Their size is usually small, so small in fact that they may be readily overlooked, but occasionally they reach larger dimensions. Microscopically the ulcers are characterized by hemorrhagic bases, undermined edges, and an entire absence of leukocytic infiltration about them. The base of the ulcer is usually formed by the submucosa, and is covered by a layer of necrotic material rich in red blood cells. Five of our cases showed these lesions, and have accordingly been placed in this group. In 2 of them worms were found in the ulcers.

4. In the fourth group we have placed the gangrenous appendices which have contained oxyurides. Despite long serial sections no specific lesions could be found in any of them, and they differed

in no respect, except for the presence of worms, from ordinary gangrenous appendices.

In addition to the changes described we have seen in the appendix two other phases of the oxyuris lesion. The first was encountered but once. It consisted of a hyaline oxyuris buried deep in the submucosa, surrounded by a few fibroblasts and a thick capsule of connective tissue. It is a specific healed lesion in which the host has overcome the parasite and is, so far as we know, unique. The other is a healing lesion and was also found but once. It consisted of the remains of an ulcer, surrounded by granulative tissue, and reduced to a mere slit.



Fig. 5.—Invasion of lymph follicle by a male oxyuris and secondary bacterial infection, with necrosis and dense infiltration of polymorphonuclear leukocytes. $\times 107$.

LESIONS CAUSED BY THE TRICHOCEPHALUS. We have encountered only 2 cases of trichocephalus appendicitis, 1 catarrhal and 1 gangrenous, but definite lesions corresponding with those described by other observers were found in both of them, and they may therefore be briefly described as characteristic trichocephalus lesions. In the gross a typical trichocephalus appendix appears like an oxyuris appendix. The microscopic picture differs in that the whip-worm does not burrow so deeply as the pin-worm, but, having penetrated the mucosa, tunnels along immediately beneath it, raising it in a fold and thinning it out so that it at first appears to be an extra coat of the worm. Fig. 6 shows a trichocephalus burrowing under the columnar epithelium. The lesion is character-

istie and, like the oxyuris lesion, is entirely free from leukoeytic infiltration.

The question naturally arises whether the worms produced the symptoms in the cases in which we were unable to demonstrate specific lesions. We believe that in these cases, too, they have been the exciting cause of the disease, not simply by the irritation set up as foreign bodies, although this may have been their mode of



FIG. 6.—Invasion of mucosa by trichocephalus. A thin membrane of reflected epithelium is seen about part of the parasite. $\times 107$.

action, but very probably by causing minute puncture wounds of the mucosa, which we have been unable to find. It is rather remarkable that the four appendices from adults all failed to show specific lesions. A possible explanation is that inasmuch as most of the lesions fail to produce a local inflammatory reaction, they might heal without going through the stages of repair and scar formation, thus leaving no trace of their existence behind them. In the gangrenous appendices the process may have been initiated by bacteria which gained access through parasitic lesions. Extensive

gangrene would preclude the possibility of finding specific lesions in these cases.

We have thus demonstrated in 13 out of 19 oxyuris or trichocephalus appendices, removed from children for clinical signs of appendicitis, definite lesions which we consider specific for these parasites. In 4 adult cases and in 3 autopsy cases in children no specific lesions were found.

SYMPTOMATOLOGY. In considering the symptomatology of the disease we will disregard the gangrenous cases, for in them, except possibly in respect to the previous history, the picture does not differ from that of any gangrenous appendicitis. Reference to the table shows that less than 15 per cent. belong to this variety. It is of the non-suppurative verminous appendicitis, the remaining 85 per cent., that we wish particularly to speak, for we believe that in a certain number of these cases a positive diagnosis of appendicitis due to worms can be made before operation.

In cases of appendicitis, especially in children and young adults, the patient should be questioned closely for symptoms of worms, whether they have ever been noticed in the stools, as to anal or nasal itching, capricious appetite, etc. In children the mother may give a history of the child's restless sleep, some loss of weight, or some reflex symptoms due to irritation of the genitalia. In female children there may be a vaginitis. It is surprising, however, in how few cases worms have ever been noticed by the patient or mother. The bowels may be normal, constipated, or loose. Constipation has not been particularly noted in our series. Andrikidis² remarks how frequently, in ordinary intestinal infestation with trichocephalus, attacks of abdominal pain with vomiting and diarrhea and a slight elevation of temperature are seen. The presence of worms or their eggs in the stools or a history of their having been previously seen is not necessarily an indication of parasitic appendicitis. We have recently had such a case in a child in which we both concurred in a diagnosis of parasitic appendicitis, but in whose appendix no worms or parasitic lesions could be found. This appendix showed catarrhal inflammation, and it is possible, as we have before mentioned, that the worm had escaped into the cecum leaving behind no visible lesion. This is in agreement with Cuthbertson, who thinks that many cases of catarrhal appendicitis with a history of only one attack are caused by intestinal parasites.

The character of the pain in parasitic appendicitis is sometimes quite distinctive. It has frequently been described as a gnawing, scratching, itching sensation in the right lower quadrant of the abdomen. In addition to this there are usually the attacks of severe pain, first localized, then general abdominal, as seen in other forms of appendicitis. Hanley's patient complained of a cramp-like, tingling sensation in the appendix. Martin and Pabouf and Dubois⁴⁷ lay emphasis on the character of the pain, which

they say resembles the sensations caused at the anus by pin-worms. Pabeuf and Dubois describe the attacks as of short duration, but in our own cases this point has not seemed particularly evident. We have noticed, however, that the pain is frequently out of all proportion to the objective symptoms and Carson thinks the attacks are characterized by an exaggeration of subjective symptoms and a comparative absence of physical signs. Pain has, in all cases, been a marked feature. The character, severity, duration, or frequency of the vomiting has not seemed to us to differ from that seen in cases of non-parasitic appendicitis, and it has been present in all but three of our cases.

On examination the patient is usually found to be a child, for the disease is essentially one of childhood and early adult life. There is frequently some anemia, but the patient, though perhaps under weight, does not, as a rule, appear very sick. The temperature has varied from normal to 103.8° , the average being about 100.5° . This does not agree with the statement of Oppe, who says there is no fever; or with the statement of Erdman that the temperature is 104° to 105° for twenty-four hours, then falls to about 99° , to be followed in a day or two by a second elevation of temperature of 1° or 2° . The pulse rate usually follows the temperature. The leukocyte count has varied from normal to 26,000 per cmm., the average being about 11,000. The polymorphonuclear cells have ranged from 42 to 87 per cent. of the total count, the average being just a little above the normal. In only a very few cases has a differential count to determine the proportion of eosinophiles been made. Where such a count has been made the percentage has been well within normal limits, except in the case of one child, aged nine years, whose appendix contained a number of oxyurides and in whose stools the ova of trichocephalus were found. The differential eosinophile count in this case was 44 per cent. This seems of interest, as trichocephalus infestation is known to give an eosinophilia while infestation with oxyuris does not.

Tenderness is, as a rule, marked on both superficial and deep pressure. In those cases which have come under our observation before operation there have been well-marked zones of cutaneous hyperesthesia corresponding to those described by Head for the appendix. Tenderness is so acute that frequently the patient voluntarily contracts the abdominal muscles, but true rigidity is so often absent that we have considered it as one of the important signs for differentiation of the disease from non-parasitic appendicitis. We have no explanation to offer for this other than that the disease is always an endo-appendicitis, with lesions confined almost exclusively to the mucosa. Carson⁹ has also noted this lack of rigidity, but in most of the reports in the literature rigidity is mentioned as one of the symptoms presented by the case. We believe that if the cases were slowly and carefully examined with

this point in view, fewer cases showing rigidity would be found. There has been practically no distention in any of our cases, no paralytic ileus, and no masses. We have unfortunately not had the opportunity to examine the stools of many of our patients either before or after operation, but we agree with Metchnikoff that the examination of a single stool is, if negative, valueless. We discovered one oxyuris appendix in the early part of our study in a rather novel way. We had at first been unable to find any oxyurides in this appendix, but a few days after operation we found an oxyuris in the patient's urine, and a more careful examination of the fecal contents of the appendix disclosed oxyurides there also.

The most important points then in making a diagnosis of appendicitis due to oxyuris or trichocephalus are the age of the patient (childhood and adolescence); the history, suggestive or definite, of worm infestation; the character of the pain; the slight general constitutional reaction, and the relative exaggeration of subjective as compared with objective symptoms. There is one further suggestion in diagnosis which we would like to offer, a suggestion not original with us, but made in 1901 by Metchnikoff. In any so-called "epidemic" of appendicitis the stools of the patients should be searched for intestinal parasites or their ova. In 1896 Goluboff²⁵ reported an "epidemic" of appendicitis in a boarding school in Moscow, and argued that appendicitis was a specific disease, sometimes contagious. Metchnikoff in his paper aptly suggests that Goluboff might have changed his opinion if he had made careful examinations of the feces.

PROGNOSIS. It has not been ascertained whether appendectomy in parasitic appendicitis causes a permanent disappearance of the parasites from the intestinal tract, and we have not as yet made any postoperative study of our cases on this point. Bearing in mind, however, the findings of Still, it would seem that appendectomy must in some cases relieve the intestinal tract from a constant source of reinfection.

In 43 cases of appendectomy in which the outcome of the operation was stated there were 4 deaths, or a mortality of 9 per cent.; 3 of the 4 cases were children. A study, however, of a large series of cases would probably show a mortality much less than this, for there is no apparent reason why appendectomy in parasitic appendicitis should be a more dangerous operation than appendectomy in appendicitis of bacterial origin. Indeed, the former when of the usual catarrhal type should be a safer operative case than the latter.

TREATMENT. Granted then that appendicitis can be caused by *Oxyuris vermicularis* or *Trichocephalus trichiura*, what is the rational treatment? Brumpt believes that medical should precede surgical treatment. Metchnikoff⁴¹ records 3 cases, clinically

appendicitis, showing infection, with both ascaris and trichocephalus, all treated medically and all recovering. The first was a girl, aged nineteen years, who had had attacks of appendicitis for ten months. Eggs of ascaris and trichocephalus were found in the stools. Vermifuge treatment was given for four months, and at the end of that time no ova could be found. The patient was kept under observation for four and a half years and had no further attacks of appendicitis. His second case was in a child, aged twelve years, in whom the same parasites were found. This patient was relieved by vermifuge treatment and was under observation for three years without further attacks. The third case was that of a man, aged twenty-three years, who had had attacks of appendicitis for four years. His mother had died of the same disease and his sister had attacks similar to his. The feces of both the patient and his sister showed eggs of ascaris and trichocephalus. This man was treated as were the first 2 cases and was well for eight months, when he was lost sight of. In addition to these cases of Metchnikoff, Oelnitz⁴⁵ reports 21 cases of appendicitis in which trichocephalus or its ova were found in the stools. All of these cases were treated with thymol, none of them were operated upon, and all recovered and had no further attacks.

These cases suggest that there is a considerable margin of safety in the medical treatment of parasitic appendicitis. But even after finding the parasite in the stools we cannot be sure that a worm has initiated the appendicular disease; and even if we knew that a parasite were puncturing the mucosa of the appendix we could not be sure that secondary bacterial invasion had not taken place and that gangrene, perforation, and peritonitis would not be the ultimate result. Clinicians universally have long recognized the fact that the oxyuris of all the intestinal parasites is the most difficult to permanently dislodge from the intestinal tract. We have been unable to find in the literature a single case in which a person showing oxyuris or its ova in the feces and having attacks of appendicitis has been cured of his disease by medical treatment. The worm is so small that it can lodge in the appendix and presumably remain there for a long time. Especially could this be true of an appendix which was kinked or had a constriction at or near its base. As we have before stated, oxyurides are usually found in numbers in the appendix, and in practically all the cases both male and female parasites have been present. The trichocephalus, on the other hand, usually occurs singly in the appendix, although occasionally more than one parasite may be found. Girard's²⁴ case contained one trichocephalus of each sex. How easily then could parasites, more particularly the oxyuris, live and breed for years in an appendix, forming a constant source of reinfection to the intestinal tract, and causing from time to time attacks of appendicitis. Very little is known regarding the action

of cathartics on the appendix, and we doubt whether anything is definitely known regarding their ability to cause the appendix, normal or pathological, to completely empty itself. We cannot therefore agree with those who advocate medical treatment for cases of appendicitis in which parasites or their ova are found in the feces, for to our mind the possibility of obtaining permanent relief by this method is in the majority of cases rather remote. Appendectomy when possible seems to us the treatment of election, for by its means the individual is relieved of an ever present menace to health.

CONCLUSIONS. 1. There is a definite and characteristic form of appendicitis produced by *Oxyuris vermicularis* or *Trichocephalus trichiura*.

2. The disease is comparatively common, constituting 15 per cent. of the 129 cases of appendicitis in children, which have been the basis of the present study.

3. The typical pathological changes consist of a catarrhal type of inflammation, and punctures and ulceration of the mucosa of the appendix by the parasites.

4. The clinical picture is dominated by the exaggeration of subjective and lack of objective signs. Rigidity is frequently absent, and is almost always noticeably less than would be expected from the acute degree of tenderness present. In some instances the parasites or their ova may be demonstrated in the feces.

5. The ideal treatment is appendectomy.

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PROBLEMS IN THE TREATMENT OF EXOPHTHALMIC GOITRE.¹

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SHORTLY after beginning the practice of medicine I had the opportunity of seeing and of attending, until her death, five years

¹ This paper was read in its present form before the Cooke County Medical Society, Chicago, January 31, 1912. The intention of the author to amplify it was never carried out. The paper is published, therefore, without the contemplated corrections and additions

later, a woman aged fifty-eight years, who for twenty years had been classed as "nervous" and who had, it was said, a pronounced nervous heart. The clinical picture of this individual is as clear to me today as it was thirty years ago. She was emaciated, tremulous, slightly but uniformly pigmented, with full protruding eyes and had a small, hard goitre, of which the right lobe was the larger, was subject to profuse sweats and diarrhea, had a fickle appetite and uncertain digestion, a constant tachycardia, palpitation with or without provocation, and dyspnea due to slight causes. Her disability was extreme and death, after months of cardio-vascular distress, was a welcome relief. Owing to her long period of invalidism her household was subservient to her, and about her its affairs revolved; its every thought and action depending on the possibility of weal or woe to the patient.

How many of these cases are seen, and how many years of otherwise useful activity are lost, can never be told. We know more about this condition today and to spare invalidism of this form is now considered to be the goal of both physician and surgeon, but the duty, perhaps of the former rather than the latter.

Thirty or forty years ago an invalidism of this type was attributed too frequently to nervousness, and in that convenient repository, these cases were cast and the individuals allowed to work out their own destiny without much medical aid; their comfort depending only too rarely upon the sympathy and resourcefulness of the medical advisor. Fortunate was the patient whose physician took a large view of the situation and mercifully saved the patient from the innuendoes and jibes so frequently the lot of the individual with alleged nervous disease.

The failure of the internist in the past to aid such individuals resulted in stimulating the interest of the surgeon. So active have been the efforts of the latter that in the present day it is the general belief that exophthalmic goitre is a surgical disease. It may be said without question that as long as the surgeon limited his efforts to the relief of the physical deformity associated with the disease he was acting within his domain. In many such cases, surgical intervention, aside from removing the deformity, gave a relief to the phenomenon which are now known to be due to hypersecretion of the thyroid gland. It was natural therefore, that such results, coupled with those of experimental pathology and experimental surgery, justified the surgeon in going as far as he would. That he has gone far is shown in the prevailing opinion concerning the necessity of surgical interference in this disease. This impression has gained ground because, on the one hand, of the numerous favorable results following operation, and on the other hand, because of the widely differing opinions among internists concerning the medical treatment.

Let us see whether the facts justify the position of the surgeon.

He is to be credited justly with the development of a splendid technique and with the reduction of operative mortality to a very small figure. But as to the ultimate result there remains some doubt. When we hear of a surgeon operating on a thousand or more cases and a score or more surgeons reporting their hundreds, the thoughtful observer, and especially the internist of experience, pauses to inquire: Is surgery successful because the internist has been lacking in his efforts as to general treatment? An answer to this question is difficult. One should know the course and death rate of exophthalmic goitre and of a variety of complicating conditions. These are lacking. The fact, however, remains that the problem is not the reduction of the death rate, but the prevention of invalidism, for such statistics as are available give the impression that death from exophthalmic goitre is not a frequent occurrence. The rate in medical practice is not much, if any, higher than the surgical death rate of three per cent. (this of course excludes death from mechanical causes which should never be allowed to occur). That the important problem is the avoidance of invalidism cannot be denied. In this connection, the details of the clinical histories of a few individuals, may be illustrative.

CASE I.—A woman, now aged forty-five years, was at the age of twenty desperately ill with symptoms of extreme hyperthyroidism, and for months severe nervous phenomena compelled confinement in an insane asylum; at times death seemed imminent. After a year of general medical treatment complete recovery took place. Ten years later she was still in normal condition. Four months ago hyperthyroidism in pronounced form returned, but with treatment by rest and care all symptoms disappeared. She is now suffering from pronounced myxedema. This is the third case of such swing of secretory activity from plus to minus that I have seen. Would the myxedema have developed earlier had a portion of the thyroid gland been removed early in the disease? Do we know enough of the results of present day surgical treatment of exophthalmic goitre to know that this change is not a remote possibility of operative interference?

CASE II.—When aged twenty years, Miss S. had pronounced hypertrophy of the thyroid gland with excessive secretion, characterized by such symptoms as tremor, tachycardia, nervousness, diarrhea, emaciation, and exophthalmos. After three years of continued treatment all symptoms of hypersecretion disappeared; the enlargement of the gland and exophthalmos remained. The patient has since married and has four children.

CASE III.—A business man, aged fifty years, presented, in 1897, enlargement of the gland with extraordinary symptoms of hypersecretion. A vicious life and an unusually harrassing experience in the stock exchange preceded the symptoms and the history showed a possibility of the disease having first developed at the

time of long residence in a goitre district of Michigan. The heart was very dilatable, the orifices enlarging and contracting from week to week; an aortic regurgitation appeared and disappeared. Many months of treatment were followed by a cure without return of symptoms until the present time.

Other histories might be quoted to show that it is wise to delay, or at least not to decide hastily, on the question of operation for endemic exophthalmic goitre. Many of my cases are too recent to report in final form, but my records show that with purely medical treatment a number have been cured and have remained well for six years or more.

Many minor points, it seems to me, are not infrequently ignored, or too lightly valued by advocates of surgical treatment. The latter is too frequently adopted without testing first the value of general treatment. Also, it is sometimes of value to try the effect of drinking water different from that of the locality in which the patient has lived during the development of the disease, and again it is well to remember the relations, as emphasized in the earlier papers of McGraw of Detroit, which are now well nigh forgotten, of uterine and ovarian functions and of pregnancy to the secretion of the thyroid gland. My cases falling in this group are not many, but I have occasionally been impressed by the improvement of the thyroid condition after organic or functional disorders of the reproductive organs have been corrected. As an example of such improvement the following case is illustrative:

Mrs. L., five years ago, had a large fibrocytic goitre with hypersecretion and operation was necessary to avoid strangulation by mechanical pressure. Two years later the secretory symptoms returned associated with menorrhagia, and symptoms of prolapsus uteri. It was the general opinion of those who had seen the patient that it was wise to operate on the goitre and the pelvic disease at the same time. The writer believed that the latter operation would be sufficient and this alone was done; as a result all symptoms of goitre disappeared. Recently, however, after a period of a severe mental strain and anxiety the secretory symptoms reappeared, but not with the same severity as before.

In a second case, Mrs. S., symptoms of marked hypersecretion of the thyroid were accompanied by a uterine disturbance, inflammatory in nature; treatment of the latter by a gynecologist led to disappearance of the pelvic trouble as well as the symptoms due to the thyroid.

After having observed many cases of exophthalmic goitre under various circumstances, the question to my mind is whether or not *any* violence to the system may not bring about temporary or even permanent relief of the symptoms. Thus, in one instance, the poor sufferer who had twice been operated on by Koehler, lost his eye by an explosion of fireworks. The eye had to be enucleated.

However, in spite of this terrible experience, the favorable progress of the thyroid condition was unaffected.

In another instance a woman aged sixty years, showed severe, symptoms of hypersecretion for five years; for two years she was in bed nearly all the time because of weakness and a bad heart. While bed-ridden appendicitis with abscess occurred, and the surgeons declined to operate. Rupture into the bowel took place and she was ill four weeks. Following this illness, such improvement in her hypersecretory phenomena occurred that she was able to walk about, and for two years she enjoyed as much relief as we often see after a thyroid operation, and as compared with her condition during the preceding two years, she was practically well. At the end of two years a bronchopneumonia developed, thyroid symptoms recurred, and recourse was had to serum, but to no avail. The question, therefore, arises, are operations on the thyroid beneficial because of the operation *per se* (White)?

The object of these remarks is to reinforce the principle, admitted by surgeons, that medical treatment, having for its object the restoration of the functions of other portions of the body is more frequently available than surgical treatment; in short goitre is not a surgical disease.

I do not make this statement to decry surgery for I have had operations performed on many individuals, as for example, those who will not or cannot take time for a long medical treatment. Indeed, I am prepared to say that with the present day knowledge which the laity possesses of the surgical treatment and with a knowledge of the uncertainty of the clinical course of the disease, it is unwise to assume the responsibility of denying surgical treatment until the patient has at least had the advantage of surgical opinion and experience. For this reason I have had many operations performed, but I am neither satisfied or dissatisfied with the results. Hence the question that ever occurs to me: Is there not more for the internist to do? There is no great amount of evidence that the surgeon himself is entirely satisfied. That surgical treatment does not obtain in the great majority of cases many surgeons admit, Charles A. Mayo endorses the statement of Kocher² that 90 per cent. of all goitres can be so improved by medical treatment as to make operation unnecessary. Coupled with this is the fact that Kocher has operated upon 4600 cases of goitre; in addition, in his enormous experience he has found only 780 cases of exophthalmic goitre which required surgical treatment.

These fragmentary observations, and somewhat disconnected statements, may be summarized in the following conclusions which represent the convictions of the writer:

² Bull's System of Surgery.

1. Endemie goitre should not be treated surgically until proper general treatment has been employed for a long period.

2. Surgical intervention should not be advised in cases of goitre associated with functional or organic disturbances of other secretory organs until the associated disorders are removed or relieved.

3. If relapse occurs in spite of general treatment, or in spite of treatment directed against the disorders of other organs, a goitre should then be treated surgically.

4. Medical treatment should be continued from six to twenty-four months. Favorable results should not be promised unless the patient is under the absolute control of a physician so that treatment by rest, diet, bathing, physical therapy, and so forth may be carried out with precision and continuity.

5. Surgical intervention requires the same rigid and prolonged after treatment to give permanent results.

Finally, my conviction is that the surgeon does too much and the internist too little in the treatment of goitre.

THYROID DISEASE COMPLICATING PREGNANCY AND PARTURITION.¹

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IN the present stage of our knowledge we recognize thyroid disease as degeneration, principally colloid in character, of the thyroid gland, resulting in deficient action and secretion, or excessive activity of the thyroid, producing an unusual quantity of thyroid secretion.

The relation between activity of the thyroid gland and functions of the genital organs in women has long been recognized. Cases of thyroid enlargement in girls at puberty frequently come under the observation of the general practitioner. Under favorable conditions the firm establishment of good general health is accompanied by the disappearance of enlargement of the thyroid.

In pregnancy, Frommer² has reviewed the work of Vassale in the *Italian Archives of Biology*, 1905, the *Reforma Medica*, the *Proceedings of the Medico-Chirurgical Society of Modena*, and his paper on "Tetanus," published in 1898.

By experiment and by dissection Frommer demonstrated the function of the parathyroid bodies in their production of toxins

¹ Read before the Alumni Association of the Lying-in Hospital of New York, February 13, 1912.

² Monats. f. Geburts. und Gynäk., 1906, Band xxiv, Heft 6.

causing eclampsia and tetany. He found these bodies small, oval, round, solid masses, 2.5 mm. to 15 mm. in diameter, yellowish red in color, and slightly harder than the lymphatics. There are two upon each side of the inner aspect of the lateral masses of the thyroid. These observations were confirmed by Humphry. In the majority of cases no colloid material was found in the parathyroids. Vassale believed that the thyroids are trophic glands, the parathyroids producing an antitoxin.

Frommer concluded that the parathyroids are epithelial organs, having an antitoxic function, whose interruption is followed by tetany, and that pregnancy and labor vitally influence the performance of their functions. When both thyroids and parathyroids are removed, fatal tetany follows. With the partial removal of the parathyroids and implantation of placental tissue, acute toxemia is produced. There is abundant clinical evidence to show from many sources that in many cases of the toxemia of pregnancy the thyroid is diseased. The administration of thyroid extract favorably influences some cases of toxemia, and assists in averting eclampsia; while in other cases the remedy produces no result. In Vassale's experience even the presence of syphilis did not prevent the favorable action of thyroid extract in the toxemia of pregnancy.

The association of pregnancy with exophthalmic goitre has long been recognized. Reviewing only the recent literature of the subject, Audebert³ reports the case of a patient in her second pregnancy suffering from exophthalmic goitre and toxemia, although the urine contained no albumin. A milk diet produced temporary improvement, but the patient grew suddenly much worse with a very rapid pulse, and was relieved temporarily with wet cups. Coma followed, for which bleeding was done. Labor ensued, and a feeble, living child was delivered by forceps. The patient improved considerably after labor, and finally made a good recovery upon an absolutely milk diet.

The administration of thyroid extract in tablets produced no effect, but the exophthalmic goitre which had persisted for ten years completely disappeared.

Charbin⁴ and Christiani report the case of a patient who had suffered for three years with myxedema and exophthalmic goitre. The extirpation of the thyroid was followed by an increase in myxedema, for which small portions of fresh thyroid gland were implanted beneath the skin, with a favorable result. A pregnancy supervened, which proceeded to a normal termination.

Potte and Kervally⁵ describe an interesting autopsy upon a patient who died with eclampsia. The renal lesions were considerable, and the liver was not much changed. The thyroid

³ *Annali di Ginecologia*, September, 1906.

⁴ *Gaz. des Hôp.*, 1906, No. 78.

⁵ *L'Obstétrique*, July, 1907.

gland was greatly enlarged, microscopic examination showing fatty degeneration, cystic dilatation, and the free formation of colloid material.

Fry⁶ reported an excellent result from the administration of thyroid extract in a patient whose nitrogenous metabolism was greatly disturbed during pregnancy. A normal labor followed.

Gottschalk⁷ describes the case of a patient suffering from a goitre so large that it caused severe pressure symptoms by interfering with the larynx and respiratory passages. The patient had never been pregnant. After the removal of the enlarged thyroid conception occurred, followed by a return of the pressure symptoms. Premature labor was induced at seven months, during which the patient suddenly died, apparently from shock.

Kron⁸ reports 2 cases of exophthalmic goitre in a mild degree, which became much worse during pregnancy, and improved after labor. Kron believes that in the first half of pregnancy thyroid disease exercises a very unfavorable influence upon the embryo; but in the second half of pregnancy he considers the mother more in danger.

Lichtenstein⁹ reported before the Obstetrical Society of Leipsic, a fatal case of exophthalmic goitre in a pregnant woman. The patient had passed through two pregnancies successfully, with no marked enlargement in the thyroid. A sister died of heart failure during pregnancy, another sister suffered from exophthalmic goitre. During the third pregnancy Lichtenstein's patient suffered from difficult breathing and pronounced tachycardia with exophthalmos, which developed rapidly.

On admission to the hospital her pulse was 140, the circumference of her neck, 42 cm., she was edematous, and with 2 per cent. of albumin in the urine. The uterus was gradually dilated, and without much difficulty a dead child was extracted by the breech. This was followed by a second, both fetuses being about six months advanced. The patient died in apparent collapse on the day following her delivery.

Croom¹⁰ believes that the physiological swelling of the thyroid gland in pregnancy seldom passes to the point of exophthalmic goitre or severe disturbance. In his experience most patients who have exophthalmic goitre before conception are not made materially worse. The observation that many of the children born from these mothers are neuropathic does not, in his mind furnish an indication for the interruption of pregnancy, his view of the subject being essentially a conservative one.

Resinelli¹¹ reports 5 cases of exophthalmic goitre complicating

⁶ Amer. Jour. Obst., October, 1907.

⁷ Berl. klin. Woch., 1907, Nos. 50 and 51.

⁸ Zentralbl. f. Gynäk., 1908, No. 28.

⁹ La Ginecologia-Firenze, 1908, Anno 6, Fasc. 2, p. 62.

¹⁰ Medicin. Klinik, 1907, No. 3.

¹¹ Edinburgh Med. Jour., 1907.

pregnancy, in all of which pregnancy produced a great increase in the severity of the disease. In 2 cases pregnancy was prolonged to its natural termination; in 2 cases labor was induced; and 1 case terminated by the spontaneous expulsion of a small and macerated fetus.

In the light of our present knowledge, Charcot's opinion that pregnancy sometimes improves these patients must be considered as erroneous. In Resinelli's experience a careful regulation of hygiene, the use of electricity, and especially the Röntgen rays, and the administration of antithyreodin are indicated; if evidence of kidney failure supervenes and the patient has reached the seventh month with a living fetus, labor should be promptly induced.

Skutsch¹² reports the case of a woman, aged thirty-nine years, in her fourth pregnancy, married five years. During her first labor the thyroid gland enlarged, but afterward diminished in size, and in the second and third labors was not perceptibly enlarged. In her fourth pregnancy exophthalmic goitre developed rapidly; the symptoms were relieved by large doses of bromide of sodium. Nutrition failed, and during the last weeks of pregnancy the patient lost strength and became melancholic, fearing that she would die as a sister had previously died from exophthalmic goitre. Labor developed spontaneously with the expulsion of dead twins, at about six months' development. There was little hemorrhage, but on the following day, after great restlessness and coma, the patient died.

Skutsch cannot believe that pregnancy in itself causes exophthalmic goitre. He believes that individual cases vary greatly as to the development of dangerous symptoms. There can be no question, however, but that the disturbance in metabolism caused by pregnancy is very dangerous to a patient having exophthalmic goitre, or having a predisposition to it. He considers the great disturbance in the action of the heart as especially dangerous. He positively denies the opinions previously advanced by Charcot, Carlein, Trousseau, and Sonza-Leibe, that pregnancy ever influences exophthalmic goitre favorably.

Massini,¹³ of Buenos Ayres, has studied the influence of thyroid conditions upon eclamptic convulsions. His experiments show that while three-fourths of the gland may be safely extirpated in non-pregnant bitches, in pregnant bitches the same operation is followed by severe convulsions.

Ward¹⁴ reviews extensively the literature of thyroid disease and reports fully the interesting case of a primipara at the end of the third month, married six years; two miscarriages, spontaneous

¹² Zentralbl. f. Gynäk., 1908, Band lxxviii, p. 917.

¹³ Paper published in Spanish and reprinted in *L'Obstétrique*, 1908, No. 5.

¹⁴ *Surg., Gyn., and Obst.*, December, 1909.

at the third and fourth weeks. The family history showed exophthalmic goitre. The patient, when aged twelve years, had nervous symptoms of the disease manifested later on by tachycardia. This was improved by the use of cytotoxic serum and thyreoglobulin. Curetting was performed. This was followed by a marked return of the symptoms, which subsided under the serum treatment. Pregnancy ensued. The patient was decidedly nervous and restless, with moderate hypertrophy of the thyroid, constipation, and morning sickness. Injections of thyreoglobulin appeared to be beneficial until the end of the fifth month, when the urine greatly diminished, headache and vomiting becoming severe. In the sixth month a nitrogenous partition showed ammonia, creatinin, and rest nitrogen, greatly increased, with diminished urea. During the first two weeks of the sixth month the dose of thyreoglobulin was increased to 10 minims, twice daily; then three times daily, acting almost as a specific. The urine increased following the injections. During the seventh month the patient was very ill, with exhaustion and greatly diminished nitrogenous excretion. In the eighth month it was thought impossible for the pregnancy to proceed, and labor was induced by manual dilatation and bags. Dilatation being difficult, vaginal hysterotomy was performed, and a feeble child, weighing 6 pounds, was readily delivered by forceps. The placenta was adherent and was extracted. The patient rapidly recovered. The child lived thirty-six hours, dying from intracranial hemorrhage.

Ward calls attention to the use of a saline extract of thyroid proteids made from fresh normal human glands as being more efficient than sheep thyroids, as ordinarily prepared. The hypodermic method he considers much superior to administration by the mouth.

Seitz¹⁵ reviews previous experiments upon the relation between disease of the parathyroid bodies and eclampsia. His studies led him to conclude that during pregnancy the parathyroids become softened, more vascular, with an increase in the chromophile cells. In eclampsia these cells are lessened or disappear. Connective tissue increases, fatty colloid material and cysts develop. In some cases tuberculous infection has also been present. He believes that one must sharply distinguish between tetany in pregnant animals produced by partial or total removal of the parathyroids, and eclampsia. The so-called eclampsia of animals as seen in the cow he considers tetany and not true eclampsia. Nor does he believe that extract of the parathyroids can be successfully used in eclampsia.

Stowe¹⁶ brings an interesting point into the study of this subject in reporting the case of a young woman in her second pregnancy, who a year previously had an abdominal section for acute appendi-

¹⁵ Arch. f. Gynäk., 1909, Band lxxxix, Heft 1.

¹⁶ Amer. Jour. Obst., May, 1909.

citis, at which miliary tuberculosis of the peritoneum was also found. She had an abortion caused by exophthalmic goitre which developed rapidly just before the abortion; and after abortion she suffered from slight exophthalmos, nervousness, tremor, rapid heart action, increased reflexes, and enlargement of the thyroid. This condition was somewhat improved by rest in bed, the application of ice, and the use of sedatives. When the second pregnancy occurred her symptoms became worse, vomiting developed, and the patient grew very rapidly ill, with diarrhea and bloody discharges. The urine contained 2 per cent. of albumin. The uterus was emptied by rapid dilatation, under ether, and during the next three days the vomiting ceased, the diarrhea diminished, but the patient was delirious, with incontinence of the bladder and bowels. Icterus, petechiæ, and enlargement of the liver developed, with active restlessness and twitching of the limbs, without convulsions. Death ensued, and an autopsy could not be obtained.

Bonnaire¹⁷ reports the case of a primipara in the seventh month, who had very rapid swelling of the thyroid, syncope, and paralysis of the right vocal cord. There was no exophthalmos or tachycardia. Labor was induced by introducing Tarnier's bag into the cervix. This was followed by improvement in the respiration, although labor did not develop, and the bag was removed. During the last two months of pregnancy the patient had frequent attacks of hysteria, which were ascribed to the thyroid auto-intoxication.

A second case was that of a patient in her second pregnancy who had great enlargement of the thyroid, which disappeared very largely after her confinement. In the third pregnancy the thyroid again enlarged, the right being much more swollen than the left half. Exophthalmos and dilatation of the heart, with disturbed circulation developed. There was also edema of the lungs, diarrhea, 4 per cent. of albumin in the urine, cyanosis, and dyspnea. An attack of syncope was followed by the patient's transfer to the hospital, when another attack so severe as to threaten her life occurred. Free bleeding improved the condition somewhat, and labor was introduced by the introduction of a bag. A living child, ill-developed and under weight, was born. The patient apparently improved, but two hours after labor she had a severe postpartum hemorrhage and collapse, from which she slowly recovered. The exophthalmic goitre remained, although less severe.

Goodall and Conn¹⁸ contribute a very interesting paper upon the relation of the thyroid gland to the female generative organs. They cite the case of a patient who had passed the menopause,

¹⁷ Presse Médicale. 1910, No. 28.

¹⁸ Surg., Gyn., Obst., May, 1911.

after normal childbirth. She lost weight, and suffered from dull, aching pain in the lower abdomen. The neck enlarged, with dyspnea, and dysphagia.

On section, chronic pelvic tuberculosis was found, the tubes were dilated with pus, the ovaries were riddled with abscesses, dense adhesions, and one pus tube communicated with the bowel in two places. The uterus and appendages were removed, the bowel closed, and the abdominal cavity drained through the vagina. Recovery was complicated by abscess, with a discharge of pus through the abdominal incision. The thyroid gland steadily decreased in size and became much smaller than normal.

Goodall and Conn have found no similar case reported in the literature. They report a case where amenorrhea was greatly improved by the administration of thyroid extract, and another where amenorrhea and epilepsy, without apparent thyroid change, were greatly improved by thyroid extract. Sterility, obesity, and menorrhagia, have also been improved in their observation by thyroid extract. In another patient hysterectomy, with the removal of the right tube and ovary, was performed for excessive hemorrhage from the uterus, with symptoms of myxedema. This patient was greatly improved after operation by the combined administration of calcium lactate and thyroid extract.

These cases are cited as those in which deficient action of the thyroid has produced disturbance in the functions of the generative organs. The case of tuberculosis complicated by thyroid disease is apparently unique. Pinard's cases of disturbed menstruation from thyroid disease are quoted.

They conclude that the relation between the female genitals and the thyroid is very intimate, and that the thyroid and ovaries mutually influence functional activity. Thyroid secretion and ovarian secretion neutralize each other, the secretion from the interstitial cells of the ovary apparently bringing the ovary and thyroid into close relation. Ovarian hyperactivity is a frequent cause of the development of exophthalmic goitre.

Porter¹⁹ reports 2 cases of hyperthyroidism in women, one of which was relieved by the administration of thyroid extract, the other by injections of boiling water into the thyroid gland. He also reports the case of a patient in labor with her fourth child, with marginal placenta prævia. On admission to the hospital the cervix and vagina were tamponed with gauze, which controlled the hemorrhage. At the end of five hours the patient became very restless, with rapid and irregular pulse. She was immediately delivered under ether of a small, poorly nourished, dead child. There was not sufficient uterine hemorrhage to account for the symptoms. On the following day she suddenly developed a very rapid, weak pulse, with air hunger.

¹⁹ Amer. Jour. Obst., 1911, No. 5.

On examination a medium enlargement of the thyroid gland was found, and it was ascertained that during her pregnancy the patient had suffered from frequent attacks of tachycardia. Porter reports other cases illustrating the general effect of thyroid disease, and in another paper,²⁰ gives the results of his treatment of hyperthyroidism by injecting boiling water into the gland. This treatment stops the excessive activity of the gland, and may give the patient an opportunity to recover sufficiently to have the gland safely removed by a surgical procedure.

In my experience it is no unusual thing to observe disturbance of the functions of the genital organs in women, associated with varying degrees of thyroid disease. At the Jefferson Maternity we have several times observed patients with enlarged thyroids who passed through labor with little disturbance, without much increase in the thyroid, with moderately well-developed children, and who made fairly good recoveries.

Among my private cases within the last few years it has been my fortune to see 4 patients in whom thyroid disease, with or without other complications, proved a critical factor in determining the life of mother and child.

CASE I.—A tall, pale, brunette. During her first pregnancy her family physician thought she had diabetes, because she had edema and sugar in the urine. Patient denied enlargement of the thyroid gland at that time. She gave birth to a healthy, male child, which she nursed thirteen months.

The first pregnancy terminated prematurely at about the eighth month. In the second pregnancy no enlargement of the thyroid was observed when the patient first came for examination. The pulse was normal, the tongue slightly furred and coated, and the patient pale. The pelvis was normal. Aside from her pallor and unusually nervous condition she presented no abnormality. An examination of the urine was negative. Spontaneous labor developed rapidly, with great excitement, the mother becoming unmanageable. Amniotic liquid was in excess. The child weighed 7 pounds and 3 ounces, and was fairly nourished. The placenta contained infarcts along its edges. The patient had an excessive secretion of milk, and nursed the child, but remained in a highly neurotic and hysterical condition. Involution proceeded fairly well, retroversion developed, the uterus being readily replaced in the knee-chest posture. At birth very slight lacerations in the anterior and posterior segments occurred, which were immediately repaired, and healed completely.

Ten months afterward the patient presented herself in wretched health. Bilateral goitre had developed with exophthalmos of moderate degree. The pulse was 130. The patient was highly

excitable, complaining of pressure symptoms and difficulty in breathing. She first noticed this condition five months after the birth of her child. She ascribed her bad feelings to a slight protrusion of the anterior vaginal wall, which she had noticed, and over which she became excessively anxious. She was urged to submit to surgical treatment for the goitre, but declined, and went to a physician, who gave her iodine. Three months later she was worse, suffering from frequent diarrhea, with headache and backache, and still possessed with the belief that her symptoms depended entirely upon the cystocele. A ring pessary readily replaced the vaginal wall. A month later she was slightly better, but would submit to no operation for the relief of the cystocele.

She passed from observation at this time. Five months later, or eighteen months after her last pregnancy, she submitted to operation at the hands of another physician for prolapse of the vaginal wall. This operation was followed by unconsciousness and delirium, in which she died. An autopsy could not be obtained. A sister also has goitre.

The significant facts in this case were the insidious development of the disease, apparently induced by two pregnancies, the first terminating prematurely after the patient had had sugar in the urine, with edema. The second pregnancy was characterized by excessive nervousness, increased amniotic liquid, slightly diminished development of the child, great excitement during labor, with hypersecretion of milk. Obstinate constipation was a factor which caused the patient to strain, and which produced the downward displacement of the vaginal wall. During the latter months of her life the patient's condition was practically that of hysteria.

CASE II.—Patient slender, fairly nourished, blonde, the wife of a professor in a college for women, and herself an instructor and lecturer on philosophy. Her early general health was good. Her first pregnancy terminated in a very prolonged and difficult labor, during which the physician in attendance considered the question of Cesarean section.

The patient first came for examination to have the presence of a pelvic deformity determined. On examination she was found to have a narrowed and flattened pelvis, with an external conjugate of $18\frac{1}{2}$ cm. The symphysis was unusually high and the vaginal tissues normal. The patient was informed that should a second pregnancy occur the life of the child would be best guarded by elective section. When pregnancy supervened the patient did well in the early months, but gradually began to suffer from nausea, exhaustion, and headache. There was slight enlargement of the thyroid, which dated from the first pregnancy, and had never disappeared. The urine showed deficient nitrogenous metabolism. The patient's condition was somewhat improved by the use of

thyroid extract and rest, the nitrogenous metabolism growing no worse. The thyroid extract was continued, with occasional intermissions, throughout the pregnancy in very moderate doses. The central lobe of the thyroid became as large as a small orange. Her general condition remained good.

The patient was allowed to go to term, when regular labor pains began, with attacks of great nervousness. She had entered the hospital a few days previously, and section was immediately performed, with the delivery of a male child, weighing between 6 and 7 pounds. During the first twenty-four hours after operation the patient was restless and exceedingly nervous. Hardened feces and fecal sand were discharged after the operation. The secretion of milk gradually formed, and the patient was able to nurse the child for some time. Six months after delivery the thyroid had increased distinctly in size. The general health was fairly good, and the patient was still nursing the child most of the time. She was advised to gradually wean the child, and enter the hospital again for the removal of the thyroid. Thyroidectomy was performed at the Jefferson Hospital by Dr. Gibbon, leaving a portion of the capsule to avoid the bad results of total removal. The patient's recovery was uncomplicated.

Eighteen months after the delivery of the child the patient was in excellent health. She was slightly thinner, but able to resume her duties as a teacher, was free from the fainting attacks which had previously annoyed her, and considered herself in excellent health. Her child had done well.

CASE III.—A multipara was brought to my attention by her sister, a trained nurse. The patient was seen at her home, giving the following history: Enlarged thyroid in the family; her parents, although having it, are living and in good health. Patient aged between thirty and forty years, moderately stout, and apparently fairly nourished. Usual diseases of childhood; mild attack of scarlatina. Menstruation began when aged between twelve and thirteen years, varying from twenty-eight days to five weeks. From twenty to twenty-three years of age she suffered considerable pain; between the ages of thirteen and fifteen years she had attacks called congestion of the brain, with headache and unconsciousness for several hours. Married twelve and one-half years, the present being her seventh pregnancy. The first pregnancy terminated in abortion at seven weeks, preceded by pernicious nausea. The second pregnancy was associated with pronounced nausea, with abortion at six weeks, said to be produced by over-exertion. In the third pregnancy, severe nausea, pregnancy terminating at seven and one-half months, the child living nineteen days, and dying with jaundice. The fourth pregnancy went to four weeks, when the patient had a violent cough which she thinks produced abortion. In the fifth pregnancy she had pernicious

nausea for five months, but went on to term, and was delivered in the hospital by the application of high forceps. She was delivered of a female child weighing $7\frac{1}{2}$ pounds, which died twelve hours after birth from birth pressure.

By examination of the patient the case was probably one of posterior rotation of the occiput. She was considerably torn, and had stitches placed in the perineum and the pelvic floor. The sixth pregnancy terminated at about the normal term, with spontaneous labor, the child being a male, weighing 8 pounds. It was allowed to nurse the mother. The child did not discharge the contents of the bowel freely, and died in twelve days, with jaundice and intestinal disorder.

The present seventh pregnancy, was characterized by nausea, which was constant, with not much vomiting. In each pregnancy the thyroid had enlarged very much, and at the time of labor had become greatly distended and occasioned pressure symptoms. When examined the patient had frontal and right-sided headache, gas in the intestine, backache, and at times swelling of the limbs. The bowels moved sluggishly. The thyroid gland was larger than it had ever been, and twice in the patient's history this enlargement had been accompanied by a marked nervous disturbance.

On examination, the right lobe of the thyroid was markedly enlarged, the neck measuring $16\frac{1}{2}$ inches in circumference. The pulse was about 90, irregular, with great variations in tension. There were no heart murmurs, nor could enlargement of the heart be detected. The head and eyes were apparently normal, the tongue broad, thick, fairly clean, and flabby. Liver dullness extended one finger's breadth below the ribs. The abdomen was tympanitic; the fundus of the uterus could not be distinctly outlined by palpation; the pelvis was of ample size and its contour fairly symmetrical. The pubes were slightly higher than normal, and the pubic arch was more narrow than normal.

On vaginal examination the promontory of the sacrum could not be reached without excessive and painful pressure. The uterus was enlarged, the lower uterine segment present, and the period of gestation about three months. The position of the uterus was normal, and there was no evidence of pelvic disease. On the right side the cervix was torn to the vaginal junction, and the pelvic floor relaxed.

The patient had been under the care of a local physician who had made examinations of the urine, reporting no casts, and no albumin. The nitrogen partition of the urine in a specimen sent three weeks before the patient was seen showed: Reaction alkaline, turbid, straw colored, specific gravity, 1016, no serum or nuclealbumin, no mucin, urea, 1.2 per cent., no casts, a few uric acid crystals, a few squamous epithelial cells. The amount in twenty-

four hours was 1700 c.c.; the total nitrogen was 11.90 grams, of which the urea nitrogen was 55 per cent., the ammonia nitrogen, 23.9 per cent., the uric acid and purin nitrogen, 1.2 per cent., creatinin and rest nitrogen, 19.9 per cent. Another specimen examined before the patient was seen showed 2350 c.c. in twenty-four hours, with a total nitrogen of 17.10 grams, of which the urea was 71.3 per cent., ammonia 11.5 per cent., uric acid and purin, 1.1 per cent., creatinin and rest nitrogen, 16.1 per cent.

A diagnosis was made of toxemia accompanied by pathological changes in the thyroid. The patient and her husband were very desirous of obtaining a living child. They were advised to put the patient under treatment, at rest, owing to the toxemic and thyroid condition, to avoid labor by elective section, as the thyroid had so enlarged at labor as to cause the patient intense suffering and to interfere with the mechanism of labor through her prostration; and when convalescent to submit to the surgical removal of the greater portion of the enlarged gland. This advice was taken, and the patient allowed to remain in her home in Ohio until the child was viable, at twenty-six weeks' gestation. She was placed upon a milk and vegetable diet, with the persistent use of thyroid extract in varying doses. Twenty-four-hour specimens of urine were sent for nitrogen partition at regular intervals. These examinations showed a gradual improvement by increase in the urea nitrogen, and diminution in the ammonia nitrogen, although the creatinin and rest nitrogen remained above normal. The patient was much encouraged by her physical improvement and very hopeful. Her pulse ranged from 104 to 108, blood pressure, 130 to 160 mm. She was able to take exercise with little respiratory disturbance. Nausea and headache disappeared; appetite and sleep improved; and the bowels moved regularly. The movements of the child became evident. The patient went on to gradual improvement, the nitrogen partition demonstrating the improved metabolism until she reached, as nearly as could be estimated, twenty-six or twenty-seven weeks of gestation. She then came to Philadelphia so that the child could be delivered, if necessary, at any time.

On examination, she was then looking well, pulse, 110 to 112, with variable but nearly normal tension. She followed strictly the diet ordered, and took one grain of thyroid extract three times daily. The thyroid was evidently larger than when first seen, but did not cause difficulty in breathing, and upon palpation, was evidently cystic. There was no edema, and fetal heart sounds were plainly heard on the left side anteriorly. The patient went on until the ninth month, when it was found that the neck had enlarged half an inch in two months. Fluid appeared in the breasts, and the head of the child descended slightly into the upper pelvis. At about two hundred and sixty-five days, as nearly as could

be ascertained, the patient entered the Jefferson Hospital, because she had been in a highly nervous and sleepless condition for several days. Edema had appeared in the lower extremities, and the patient had lost appetite and was much disturbed.

Operation was performed as soon as practicable, and a well-developed male child, weighing 8 pounds and 13 ounces, in breech presentation, was delivered by celiohysterotomy. The operation proceeded smoothly, being complete in thirty-seven minutes. The patient endured anesthesia well, without much dyspnea. She reacted well, and was very nervous and excitable during the night following the operation. The child had abundant secretion of mucus in the nose and throat, but no cyanosis, and seemed to do well. Mother and child progressed favorably after the operation. The child was not allowed to nurse, but was artificially fed, and received daily copious irrigation of the intestine, with small doses of brandy and water. For the first few days it lost considerably in weight and had abundant movements of greenish mucus. This gradually gave way to normal movements under a carefully selected milk feeding. The mother had no milk in the breasts, and at times was in a highly nervous condition. Her recovery was complicated by a stitch abscess in the lower portion of the abdominal incision, and the breaking down of subcutaneous fat. Mother and child left the hospital in good condition a month after the operation, the child weighing 10 pounds and 3 ounces. The child has steadily improved and is exceptionally vigorous and well developed.

The stitch infection of the subcutaneous tissue made its way downward to the peritoneum and infected one of the uterine stitches, the uterus evidently being adherent to the abdominal wall. Several silk stitches were passed through a small abdominal fistula, which finally closed. The mother did well after the operation for three months, when the thyroid gland became larger, and she became highly nervous and apprehensive, with loss of appetite. Menstruation had occurred twice, with considerable flow. There was no pain or distress, and the patient was able to take whatever exercise she desired.

During the last summer the patient consulted Dr. Charles Mayo, at Rochester, Minnesota, where the right lobe and isthmus of the thyroid were enucleated. It was found to be in a highly colloid and cystic condition. Following this the patient's general health has gradually improved. Her child is exceptionally vigorous and well nourished.

Delivery by elective Cesarean section before labor pains develop was selected in this case to avoid the enlargement of the thyroid, which had occurred at previous labors. This enlargement had been so great as to cause severe pressure symptoms, and to interfere with the normal action of the uterus and indirectly with the

mechanism of normal labor. Elective section was selected in the interest of the child, to avoid abnormal mechanism in labor, and the delivery of the child in an unfavorable position and presentation, through a partly dilated birth canal.

CASE IV.—Primipara, seen in consultation seven years previously. Mother had pelvic tumor and asthma. Sister in average health. The patient had suffered from pelvic pain and had abdominal section, with the removal of the greater portion of cystic ovaries and shortening of the round ligaments. Married for several years. She had despaired of having a child, and had adopted one. Shortly after menstruation ceased, and the patient had nausea, headache, edema, and albumin in the urine. There had been a bloody vaginal discharge at intervals.

On examination, the patient was between seven and eight months pregnant, no evidence of placenta prævia could be found, and the fetus was living. The mother's heart beat strongly and the pulse irregularly without much tension. The patient was unable to assimilate much food; the thyroid gland was not enlarged, but the patient was evidently toxic. Five days afterward she expelled a premature female child, weighing $2\frac{3}{4}$ pounds. The child lived forty-eight hours, having frequent attacks of cyanosis, and dying on the third day after birth.

Three years afterward the patient again came under observation, stating that since her first labor she had suffered from headache, nervous exhaustion, and astigmatism, for which glasses gave little relief. She had lost in weight. She was then four months pregnant, having bloody vaginal discharge at intervals, with polyuria, passing on one occasion 142 ounces in twenty-four hours. The bladder was very irritable, and nausea was almost constant. The patient slept poorly and was very constipated. She had attacks of jaundice, and had felt fetal life.

On examination, the pulse was rapid, with high tension. Examination of the blood showed hemoglobin, 50 per cent.; leukocytes, 6600; red cells, 3,755,000. No enlargement of the liver could be detected. There were no maternal heart murmurs. Examination of a twenty-four-hour specimen of urine showed: Acid reaction, specific gravity, 1006; pale, straw colored, turbid; no serum albumin, no sugar, no casts, and amorphous urates. The uric acid nitrogen was 73.3 per cent.; ammonia, 8.2 per cent.; uric acid, 8.5 per cent.; creatinin and rest nitrogen, 10 per cent.

The patient was placed upon a restricted diet, with a bitter and arsenical tonic, under which her condition temporarily improved. Thyroid extract, 1 grain, three times daily, was added. This treatment was continued, with little variation, for three months, the patient doing fairly well.

Labor was spontaneous, with the birth of a male child, weighing between 7 and 8 pounds. The patient was anxious to nurse

the child, and had considerable secretion of milk, which agreed with the infant. During lactation the patient had several attacks of engorgement of the breasts, with rise of pulse and temperature, and with some disturbance in the bowel movements of the child. The use of calomel, thyroid extract, and hot baths gave relief. Three months after delivery the pelvic organs were normal, the tongue clean, the breasts normal, and the patient in good general condition. The child was gradually weaned at seven months and became vigorous and fairly well developed.

During pregnancy and the puerperal state no gross alterations in the thyroid gland could be detected. The benefit following the administration of thyroid extract in the condition of mother and child was evident.

The child suffered from attacks of intermittent toxemia, which were controlled by a milk diet. The mother continued in good average health.

In this case the administration of thyroid was followed by immediate improvement in the nitrogenous metabolism, and apparently influenced favorably the secretion of milk.

The mother, who was formerly a nurse, ascribed her successful pregnancy to the prolonged use of thyroid extract.

In my experience, in examining all cases of pregnancy, the condition of the thyroid gland should receive attention. If this be manifestly enlarged or altered the patient's nitrogenous metabolism should be closely watched, and if evidences of lack of thyroid secretion be found, the active principle of the glands in some available form should be administered. I have seen the best results by small doses, 1 grain three times a day, continued for from four to seven months.

Our most reliable methods of ascertaining the patient's condition are nitrogen partition of the urine and the clinical study of the condition of the circulation. Unfortunately, pulse tension varies so greatly, sometimes under the excitement of examination, that it is not as constant and reliable a factor in diagnosis as we have hoped and wished. The nitrogen partition, in our experience, is much more reliable.

The wishes of the parents should be carefully ascertained regarding the life of the child, and the situation clearly explained to them. Where children have been lost in previous pregnancies, and the parents are desirous of offspring, all possible means should be used to continue the pregnancy, without undue risk to the mother. If there is a history of enlargement of the thyroid during labor, with the development of unfavorable mechanism and loss of the child through birth pressure, elective Cesarean section before labor should be selected.

No case should be considered as convalescent, or receiving adequate attention, in which the patient after recovery from

parturition does not seek surgical advice and treatment to permanently remedy the thyroid condition.

The induction of labor in these cases is seldom indicated as it is too slow and uncertain. The pressure of elastic bags increases the mother's nervous disturbance, and delivery of the child through a partially dilated birth canal exposes it to additional risk.

In cases where degeneration of the thyroid gland does not seem to be present, but an increased secretion of thyroid material is formed, absolute rest and milk diet, sedatives, and the application of ice over the gland, should be immediately employed, with the hope of improvement until the child can become viable. As reported cases show, it is sometimes possible to check the thyroid activity by this means, and to bring the patient to a safe and spontaneous termination of pregnancy.

FUNCTIONAL TESTS FOR HEPATIC CIRRHOSIS.

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IN its advanced state, cirrhosis of the liver is one of the less difficult conditions to recognize; but this can hardly be said of the incipient stages of the disease. One is not infrequently tempted to hazard a diagnosis of cirrhosis in those individuals described by Frerichs, "Who devote themselves too freely to the pleasures of the table and who make use of a succulent, stimulating diet, notwithstanding their sedentary mode of life;" but in the absence of physical signs opinion can amount to little better than conjecture. It is in response to a demand then that the various functional tests have been advanced, and it is the object of this paper to discuss the more important tests and their limitations.

If the present trend of ideas in physiology is in any degree correct, the liver is peculiar in the number and variety of functions that it fulfils, and these are not only secretory and excretory, but are also related to many of the finer chemical processes of metabolism, as, for example, the glycogenic and the cleavage of amino-acids. All of these activities are essentially enzymatic, and consequently it is to be inferred that any morbid process influencing the hepatic cellular nutrition would as a direct result have some bearing upon the fate of those bodies normally acted upon in the liver. The only exception logically, would be in case of hepatic functions being vicariously performed by some other organ when the liver is incapacitated through disease.

On account of the bile production appearing peculiar to the liver it was at first assumed that urobilin, because of its close chemical relationship with bile pigments, depended exclusively on the hepatic cells for its formation. A closer study of the subject, however, has shown that several other factors are to be considered; the most important, perhaps, being the reducing action of the intestinal bacteria on the bile pigments.¹ It is not definite whether the liver of itself can produce urobilin from its precursor bilirubin, or whether the former substance results only from bacterial reduction. The question must be left open for the present. Any diagnostic interpretation, therefore, put upon urobilinuria in the present state of our knowledge must be empirical rather than founded upon definite and demonstrated facts. Urobilin may be found in excess in the urine, associated not only with cirrhosis of the liver, but also with passive congestion of cardiac origin and infections involving the liver parenchyma generally.² The fact that urobilin may be increased in the urine in some diseases other than those of the liver, for example pernicious anemia, does not of necessity vitiate its value in diagnosis, since interpretation can be made in the light of other diagnostic data. The presence of excessive amounts of urobilin may be given some consideration while its absence would be ignored in the face of other evidence. In Germany particularly a certain confidence is placed in the significance of this body that is not universally felt, at least not in America. Fischler, for example, makes use of the urobilin test in estimating the degree of compensation attained by a discompensated heart. It is claimed that grades of congestion which are not to be detected in enlargement of the liver are nevertheless evidenced in a disturbed hepatic function and that urobilinuria is an expression of such an impaired activity. Fischler's observations are capable of being interpreted in another way, however, for while it may be true that passive congestion too mild to induce an increase in liver volume may impair hepatic function, it is not to be overlooked that in broken compensation there is an increased blood destruction³ and the pigments arising therefrom might also give origin to an increased urobilin excretion. Whenever there is an abnormal breaking down of the red cells of the blood, as is the case with some infections, there appears to be an increase in the formation of urobilin, which fact in some degree, at least, complicates the problem of the relation of urobilin to hepatic cirrhosis.

The urine was tested for urobilin by means of the regular tests, including the spectroscope, in all of the cases of cirrhosis mentioned

¹ Muller, *Verhand. d. Schles. Gesell. f. vaterl. Kultur.*, January, 1892.

² Fischler, *Munch. med. Woch.*, 1908, iv, pp. 1421-27; *Verhand. d. Kong. f. inn. Med.*, Wien, 1908, pp. 445-50; *Deut. Arch. f. klin. Med.*, 1908, xciii, p. 427; Arnsperger, *Beitr. z. Chir.*, 1906, lii, p. 46; xlviii, p. 725.

³ Grawitz, *Klin. Path. des Blutes*, 1902, S. 491.

in this paper, and was found present at least once in 65 per cent. of these cases. The same tests were applied to 50 urines from patients who complained of various forms of mild digestive disturbances where there was no ground to suspect liver disease in an anatomical sense, although a physiological derangement could not be excluded. In 26 instances urobilin was present (52 per cent.). It was also found in 31 of 100 urines from miscellaneous cases of various diseases of all sorts. Cases suspected of hepatic disease were excluded from this last series. In view of these results it seems conservative to assert that no reliance can be placed upon the test when one is in a diagnostic dilemma.

In this connection mention may also be made of the aldehyde reaction of Ehrlich. For some time this reaction was supposed to be due to urobilin,⁴ but it has been pretty well demonstrated by Neubauer⁵ that it is the pyrrol radicle present in urobilin that produces the color effect. While urobilin does give a rose color with the aldehyde reagent other substances which may occur in urine produce the same result. I have employed this test among others, and while there is often agreement between the aldehyde and spectroscopic⁶ tests, it is not invariably so, and on that account it seems most probable that several substances in the urine can effect this reaction.

In 1901 Strauss⁷ published a functional test for hepatic insufficiency which depends on the theory that glycogenesis of levulose is exclusively confined to the liver cells. Since the first communication this test has been extensively employed, especially in Germany, and has earned a certain respect among clinical procedures. The method of use of the levulose test, as is well known, is to give to the fasting patient, preferably before breakfast, 100 grams of levulose, dissolved in either water or tea. The urine is collected for several hours after the levulose is taken and tested for the presence of that sugar. The presence of an alimentary levulosuria is considered indicative of hepatic insufficiency. In a summary of the literature, Chajes⁸ found this test positive in 86.9 per cent. of the cases of clinical cirrhosis. The defect in this procedure lies not in that all cases of cirrhosis do not respond with levulosuria, but in the fact that a considerable percentage of normal individuals respond as well. Churchman⁹ has emphasized this point in a recent communication. He found that 9 of 38 cases, liver normal clinically, gave a positive test (23.6 per cent.), and Frey¹⁰ estimates from his experience that 10 per cent. of normal persons would give a positive test and 50 per cent. of the cases of hepatic cirrhosis.

⁴ Hildebrandt, *Zeit. f. klin. Med.*, 1906, lix, pp. 351-441.

⁵ *Zentralbl. f. Physiol.*, xix, p. 145; *Verh. Deutsch. Natur-forschr. u. Aerzte*, 1903, ii, p. 68.

⁶ For quantitative methods consult Hoppe-Seyler, *Virehow's Arch.*, 124

⁷ *Deutsch. med. Woch.*, 1901, No. 44, p. 757.

⁸ *Ibid.*, 1904, xxx, p. 696.

⁹ *Johns Hopkins Bulletin*, 1912, xxiii, p. 10.

¹⁰ *Zeit. f. klin. Med.* 1911, lxxii, pp. 383, 436.

Ten normal persons and 20 cases of cirrhosis were used in estimating the value of the Strauss test. The technique differed in no respect from that usually employed. Of the 10 normal individuals 3 responded with levulosuria (30 per cent.). It is of interest that one of these, a young man, who was induced to take the levulose a second time had no sugar in his urine on the second test. The cases of hepatic cirrhosis selected were all of an advanced type, with ascites, and were regarded as typical cases. The levulose in several instances was given two or more times. Fourteen of these cases responded with levulose in the urine (70 per cent.). Levulose was also given to a number of patients not regarded as having hepatic disease. One of these was a typical case of Charcot's hepatic fever; the Strauss test was positive, although at the time of operation (gallstones) the liver appeared normal. A young man with chronic adhesive pericarditis and enlarged liver gave a negative test, but two days later a second test was clearly positive.

In a recent communication Pari¹¹ concludes that the assimilation for galactose is so inconstant that clinical deductions in cirrhosis of the liver are very uncertain.

An attempt was made to put the whole matter of sugar tolerance in its relation to liver function on a more stable basis by resorting to animal experimentation. If the liver is indispensable for the rapid removal of absorbed sugar from the blood stream, then in dogs with Eck fistulas there should be an easily induced alimentary glycosuria. Normal dogs are capable of withstanding 10 grams of glucose per kilo of body weight without mellaturia. The tolerance for levulose was found a little higher than that for glucose. Now after an anastomosis between the portal vein and the inferior vena cava the liver no longer acts as a screen between the area of absorption and the systemic circulation (kidneys). It was observed¹² that the sugar tolerance for both glucose and levulose falls after this operation but, briefly, that levulose is better cared for than glucose. This would suggest that so far as levulose is concerned it is less dependent on perfect hepatic activity than glucose. There was also noted a remarkable fluctuation from day to day in the ability to utilize sugar as measured by the amount recovered in the urine. This bore some relation to the state of nutrition of the animal. Dogs with Eck fistulas are difficult to feed, and inevitably become undernourished after a period; and it was noted that in the later experiments, when presumably the glycogen stores of the organism were depleted, the tolerance for sugars was highest. This fact may be the explanation of some of the clinical observations.

The relation that the liver holds to nitrogenous metabolism is

¹¹ Gazz. degli Osped. e degli Clin., 1912, xxxiii, pp. 51-56.

¹² Foster, Proceedings of Society for Advancement Clinical Investigation, 1910, p. 4 to 6.

complicated and in many of its aspects by no means clear. In the first place, amino-acids resulting from the protein digestion are possibly not absorbed entirely as amino-acids, but are reconstructed into more complex bodies allied to proteins (peptids) before entering the blood stream. If this hypothesis is in any degree true it would have a bearing on results deduced from the administration of amino-acids by the mouth. When the latter bodies are perfused through the liver by means of the blood channels, however, they are broken down in several ways; arginin, for example, yields urea by simple cleavage, but is exceptional in this respect. Other acids, such as leucin and glycocoll, are primarily deamidized with the formation of urea from the amino radicle as a by-product. The formation of urea itself from these radicles is a step that is not clearly explained.¹³ In view of these experimental facts the excretion of amino-acids in the urine in the severest types of liver degenerations, yellow atrophy and phosphorus poisoning, are in a degree comprehensible, and in such conditions it matters not whether the products excreted are unchanged substances derived from digestion or are primarily autolytic. But where the liver cells are not so gravely injured as in the above states the urinary findings may be quite different. Jackson and Pearce¹⁴ found an increase excretion of ammonia with corresponding fall in urea in dogs with diffuse hepatic degeneration induced with hemotoxic sera. The absence of a marked rise in the rest nitrogen (amino-acid-N) in these experiments suggests that the liver had retained its deamidizing function while that of urea formation was impaired. It is evident from these observations with two forms of liver derangement that no deduction can be drawn *a priori* as to what function will be found predominantly deficient in human cirrhosis. Glaessner¹⁵ presumed that in cirrhosis there would be a loss in some degree of the deamidizing power of the liver and fed to patients with liver diseases amino-acids. By a method of separation which Glaessner devised he believes he has recovered from 20 to 70 per cent. of the ingested acids in the urines of cirrhotic cases, while normally none is recovered, as it is all converted to urea and excreted as such.

In my duplication of Glaessner's tests his method of recovery was not employed because it did not seem in any way reliable; the rest nitrogen in the urine offering more trustworthy results. Three severe cases of atrophic cirrhosis were studied. They were given an exclusive milk diet in definite daily amounts and all of the urine collected in twelve hour specimens. Aspartic acid was given to two individuals and alanin to one. These substances were administered in 15 gram doses before breakfast. The nitrogen partition of the urine following this experiment in none of the cases deviated from the normal sufficiently to warrant the deduction of unchanged

¹³ Hahn, Massen, Nencki, and Pawlow, Arch. f. exp. Path. und Pharm., 1893, xxii, p. 161.

¹⁴ Jour. Exp. Med., 1907, ix, 567.

¹⁵ Wien. med. Woch., 1907, lvi, p. 1034.

excretion of the amino-acid fed. These results were not encouraging, and since an autopsy on one of these cases disclosed as extreme a grade of cirrhosis as one is likely to encounter, this line of investigation was abandoned.

Recently an interesting communication has appeared from Falk and Saxl¹⁶ dealing with amino-acid secretion in cirrhosis. These authors fed alanin and glycocoll, usually the latter, and believed they recovered large percentages of the ingested substance in the urine in cases of cirrhosis. The criticism of their results rests upon their method of estimating amino-acids in urine. The method employed, that of Sörensin,¹⁷ is by no means accurate, and under some conditions the error is enormous. The choice of glycocoll (the one most used) as an amino-acid, the recovery of which was to be estimated by this method, was particularly unfortunate, since it has been pointed out that with this substance error is most liable, and most difficult to prevent.

The only way at present of determining the amino-acids in urine with any pretence of accuracy is by means of a complete nitrogen partition—the "rest" nitrogen then contains the amino-acid nitrogen. It is also necessary that the diet be the same throughout the period of observation, as this is a factor in the amount of "rest" nitrogen. With a few exceptions, the tables of Falk and Saxl are not very convincing as they stand.

While working with dogs with Eck fistulas,¹⁸ certain peculiarities in the creatin and creatinine metabolism were noticed, which suggested that perhaps these substances were sufficiently dependent on the liver for their formation to make them serve as indicators of hepatic sufficiency. It will be recalled that Mallenby¹⁹ regarded the excretion of creatin as significant of liver disease, but his cases were mostly neoplasms, wherein rapid tissue loss is a complicating factor. In my series of cases the only divergence from normal, either in finding creatin in the urine with milk diet or in the recovery of creatin or creatinine fed to patients, was when the patients had arrived at a cachectic stage in the disease. When there is a relatively rapid loss of tissue creatin appears as a urinary constituent, but this fact is not peculiar to liver disease, as it occurs in fevers also.

The fundamental question involved in securing a function test for any organ depends primarily on the discovery of some activity which is peculiar solely to the organ involved. In the case of the liver its more obvious functions, as the secretion of bile, are performed even when disease has made considerable progress, which fact is in entire accord with the number of apparently healthy cells found in cirrhotic livers at autopsy. The finer activities of

¹⁶ Zeit. f. klin. Med., 1911, lxxiii, p. 138.

¹⁷ Henricke and Sörensin, Zeit. f. physiol. Chem., 1909, lxi, p. 29; Malfatti, *ibid.*, 1910, lxi, p. 163.

¹⁸ Foster and Fisher, Jour. Biol. Chem., 1911, ix, 559.

¹⁹ Jour. of Physiol., 1908, xli, 447.

these cells, which, presumably, would be the first to suffer in diseased states, are, so far as known at present, either in part assumed by other tissues, or else the cells can endure some injury and still remain physiologically efficient. Endeavors then to elaborate tests along the lines of those discussed in this paper are hardly likely to meet with success, and particularly is this so, since what is required in clinical medicine is not only a means of confirming the diagnosis of an evident malady but especially of detecting a morbid process in its earlier stage.

THE MANAGEMENT OF ASTHMA IN CHILDREN.

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THE proper care of these cases naturally implies a knowledge of the causes, nature, and clinical varieties of asthma. The diagnosis is certainly more difficult in infants than in adults, as there is no standard whereby there can be any uniformity of opinion as to what is meant by asthma in infants. Undoubtedly many cases go astray under other names, as capillary bronchitis. The writer has often been surprised in thinking he had an acute congestive pneumonia, to find on the following day all symptoms had subsided. After two or three experiences of this kind, in the same child, one will realize he is not dealing with an inflammatory process.

Asthma is a symptom rather than a disease, and has no real pathology in the sense that there is no characteristic lesion constantly present. For this reason it is difficult to give a correct definition. Most succinct is the one given by Holt, namely: Asthma is a vasomotor neurosis of the respiratory tract. All writers agree that neurosis is the important predisposing factor, and in adults it is often the sole cause of an attack. However, in infants and children there is usually some congestion of vasomotor origin or an acute inflammation of the respiratory tract. In 20 cases of which the writer has notes, that have been under his care during the last twenty years, there was but one in which the paroxysms developed without some preceding evidence of catarrhal inflammation.

Three elements probably enter into the immediate cause of the paroxysm.

1. Spasm of the bronchioles; the muscular coat of the small bronchi consists of interwoven layers of longitudinal and circular fibers. The latter are the stronger, and under the influence of stimuli are capable of contraction with consequent lessening of the lumen. Brodie and Dixon have proved that stimulation of the

vagus by pilocarpin or electricity cause symptoms analogous to asthma.

2. Swelling of the mucous membrane lining the smaller tubes, either as an irregular turgescence or an edema, like unto that of urticaria. Further evidence of this is found in the fact that with relief of the paroxysm there is an increased secretion of viscid mucus. This mucus often contains cellular crystalline elements, although the so-called Charcot crystals are less frequent in infants than in adults.

3. The loss of resiliency of the pulmonary air vesicles whereby the residual air increases in volume, with the consequent lessening in the volume of tidal air, producing the partial stasis of air in the lungs. A striking evidence of this is the markedly distended chest, observed in certain cases. It seems to the writer most probable that this is the condition in those cases where there is a marked degree of cyanosis during an attack, and in whom there is evidence of emphysema during the intervals. It is certainly reasonable to believe that these causative elements vary in different cases, or in the same case in different paroxysms. If not, on what hypothesis are we to explain why one case is relieved by morphine, another by adrenalin, and yet another by oxygen?

When we come to study the symptoms it will be found there are three common to all cases, and when these three symptoms are associated they certainly indicate asthma.

1. The periodicity of the attacks, that is, similar attacks recurring in the same patient.

2. The dyspnea, which is expiratory in character, is in marked contrast to inspiratory dyspnea of spasmodic or diphtheric croup.

3. The wheezing breath sounds heard on auscultation and frequently audible at some distance from the patient.

Other symptoms observed in certain cases are distention of the chest, giving a full rounded appearance, the so-called barrel shape. The diaphragm is usually depressed and often fixed or immovable. It will generally be noted that the child is unwilling to talk. Even in infants the countenance has an anxious appearance, and during the severity of the paroxysm the skin is covered by a cold perspiration. The muscular effort in breathing is manifest by the play of the auxiliary muscles.

Upon auscultation there is heard a wheezing stridor, less audible at a distance from the body in infants than in children. Sonorous and sibilant rales are heard over all parts of the chest. The percussion note is usually hyperresonant. The respirations are sometimes below normal in frequency, and often the pause at the end of inspiration is shortened. In infants suffering from asthma, however, the respirations are often rapid as in bronchopneumonia. Indeed, in infants the diagnosis will often hinge upon the sudden relief of the symptoms, and tendency to recurrent attacks. A

valuable aid to the diagnosis of asthma in infants, that should be more frequently employed is the blood count. Holt in his text-book makes the following statement: "The blood picture in asthma is characteristic and has much value in the diagnosis. The important thing is the presence of a large number of eosinophile cells. They may form as high as 15 to 20 per cent. of the leukocytes. In a series of cases examined in my clinic by Wile the average was 10.7 per cent. The highest was 26 per cent. The eosinophilia is greatest at the height of the attack. The blood examination serves to differentiate asthma from simple bronchitis and tuberculosis. The existence of the eosinophilia definitely shapes the asthmatic character of these attacks in frequency."

As the management of the individual case will be influenced by the cause, a few words concerning the etiology will aid in the treatment. There is certainly an hereditary tendency. Of the 20 cases that have been under the author's care during the last twenty years, in the greater number there was a history of asthma, either in the ancestors or in the collateral line. In some cases there was a history of some nervous affection, as migraine or epilepsy, and in some cases both a neurotic and asthmatic history, and in others a distinct history of rheumatism in one or other parent. Kerley, in his book on the *Treatment of Children*, attaches much importance to the rheumatic history, and in the treatment of these cases, strongly recommends specific antirheumatic treatment.

Season has a decided predisposing influence. In the writer's experience the attacks are most frequent in the winter and spring. This applies to infants and children more than to adults, for in the latter, attacks are said to be more frequent between fall and spring. The probable reason for this is that attacks in children are usually excited by acute coryzas or bronchitis, and children are more susceptible to these catarrhal conditions during the colder and more changeable months of the year.

There are undoubtedly many exciting or reflex causes that are sufficient to induce the paroxysm, and careful search for the irritation that leads to the attack should be made in each case. There is undoubtedly some relation between asthma and eczema or other skin lesions. The writer has one child under observation who never has asthma when the eczema is active. Diphtheria antitoxin has been known to produce asthmatic paroxysms and the writer has had one personal experience of this kind in the use of antitoxin. In this case an immunizing dose of 500 units induced the paroxysm. In some cases, the paroxysms are undoubtedly caused by acute indigestion, probably due to the absorption of some toxin from the intestinal tract. Fisher, of New York, attaches much importance to this as a cause, and suggests the theory that the pressure against the stomach and diaphragm is sufficient to

excite an attack. The influence of adenoids, hypertrophied tonsils, thickened turbinates, and spurs on the septum should receive careful attention. Experience has shown that there are certain sensitive points in the mucous membrane of the nose that reflexly induce asthmatic attacks. However, it does not follow that the removal of these conditions will prevent future attacks. It is a safe rule to follow that if these conditions would demand surgical treatment in other children, they should be treated in asthmatic children. The influence of enlarged bronchial glands in causing asthma in children is difficult to determine, but it is entirely reasonable to believe that these glands may induce such attacks. Indeed, any abnormal condition in any part of the body that might in any way act as an irritant, should receive careful consideration. Children are less likely to have attacks induced by irritation of the nerve filaments in the respiratory tract, by odors from animals or plants, than adults. Also, they are less likely to be influenced by psychical impressions.

The management of asthmatic children naturally resolves itself into two divisions, namely, the care and treatment of the child during the intervals, and the treatment during the paroxysm. The asthmatic child is entitled to fair play. Each case, therefore, should receive a thorough examination, including an inspection of the entire body, noting any physical defect, with careful examination of the nose and throat. A thorough investigation should be made of the nervous and digestive systems including the diet, mode of eating, and, indeed, a physical examination of all the vital organs. An examination of the urine and a blood count should be made in each case. The history of the child and family should always be obtained. In this way valuable hints as to treatment are usually ascertained. It should be borne in mind that the treatment is directed to the patient rather than to the disease. For example, in one of my patients the only abnormal symptom gathered from a careful examination was the presence of indican in the urine. Having gathered all the facts obtainable, a careful outline of treatment, including diet, habits of the child, etc., should be specifically given to the mother. As to clothing: I would simply urge two points, namely, that the feet and legs should always be kept warm and dry, and the chest and neck properly protected to prevent catching cold. In most cases, I have found specific directions as to the diet necessary to the progress of the case. Generally a low meat diet with a high vegetable proteid. In cases induced by intestinal trouble, the diet should contain green vegetables and fruit juices. As has already been indicated, in the majority of cases the paroxysm has been induced by an acute attack of bronchitis. Hence, it is important in all cases that the mother should take prompt measures for relief upon the first symptom of a cold, as sneezing or coughing. My rule is that the child is to be

put promptly to bed, have the diet restricted to liquid foods, and given an active cathartic to move the bowels freely. Medication will naturally vary in individual cases, but hot drinks are always indicated. I have one patient in whom a dose of quinine certainly aids in aborting a cold, and another patient in whom a dose of quinine will induce a paroxysm. This has been proved several times.

There are certain cases that fail to respond to our best efforts, and in these cases a change of climate is necessary. This is often a serious problem because a change of climate may mean a change of location for the parents. From my experience in 2 cases, a change of climate for one winter was sufficient, and these cases returned to their homes and have passed several winters without recurring attacks. The writer has known of cases where a change in location of only a few miles has been sufficient to prevent the attacks. It is impossible to explain, on rational grounds, why this is true. If there is simple anemia, suitable treatment should be instituted. In cases where there is a history of rheumatism, either in the child or parents, appropriate treatment should be adopted. An instructive case of this kind will be found in Kerley's work on the *Treatment of Children*. The writer has had one case showing the benefit derived from this line of treatment. Two years have now passed without an asthmatic attack. The writer firmly believes in a system of pulmonary gymnastics for asthmatic children. The mother is instructed to give the child daily exercises in deep breathing. These exercises are to be given at regular hours, with special emphasis laid upon the importance of complete expiration. This is particularly valuable in those children in whom there is a vesicular emphysema as a result of the asthma. These children should avoid running up hill, and all violent exercises. In these cases, I wish to strongly recommend an elastic binder, worn around the chest and held in place by means of shoulder straps. This should be tight enough to exert a constant slight pressure. Its value resides in the fact that the pressure aids in expiration. Any intelligent mother can easily make this binder. The writer has personal experience with its use in 2 cases.

In many cases there is a catarrhal bronchitis, persisting after the cessation of the acute paroxysms, often with wheezing on slight exertion, and it is important to clear up this condition. In these cases the writer has found decided benefit from the use of sodium iodide. The remedy should be continued for several weeks. It should be given in doses of from 2 to 4 gr., three times daily, after meals, in essence of pepsin. There are other cases with cough, but without the nervous element, who are greatly benefited by the syrup of hydroiodic acid. The U. S. P. formula may be given in doses of from 10 to 20 minims. This is of special value where there is a general adenopathy or evidence of enlarged bronchia

glands. This remedy I have given in several cases and am convinced of its value. It is more acceptable to the stomach than other preparations containing iodine.

TREATMENT OF THE PAROXYSM. "The utter capriciousness of asthma in its response to the action of drugs, renders our course largely empirical, so that in many cases, in hope of finding one that will succeed at last, one drug after another is tried only to be discarded as useless."¹ While it is to be hoped that the modern study of anaphylaxis will shed light on prevention and treatment of asthmatic attacks, for the present, at least, the physician must be guided by clinical experience. While there is little danger to life in an acute attack, yet there is real suffering to the patient and anxiety to the parents, who naturally look to the physician for relief. In my experience the fumes from the various asthma powders do not give relief to infants, but on the contrary often aggravate the symptoms by increasing the cough. The room should be warm. Air currents are to be avoided. The condition may be made worse by changing from a warm to a cool room. At the same time fresh air is necessary. Ventilation may be had from an adjoining room rather than from open windows in the room. Only necessary attendants should be allowed in the room. If the bowels are distended with gas they should be relieved promptly by a warm enema. If the paroxysm occurs soon after a hearty meal, then a prompt emetic will afford relief.

In the writer's opinion the following cases illustrate the value of different remedies, and seem to prove that one drug will not relieve all cases. In 2 cases, the writer has given adrenalin solution hypodermically. In both cases the relief was so prompt as to leave no doubt as to the value of the remedy. On the other hand, the writer has seen it utterly fail. The dose for infants is from 3 to 5 minims of the $\frac{1}{100}$ solution of adrenalin chloride.

The writer has attended one little patient a number of times, without any remedy giving relief, until morphine sulphate, $\frac{1}{30}$ grain, was tried. Then in subsequent paroxysms this drug gave relief each time it was given. In another case chloral hydrate gave prompt relief. Other remedies had been given by me in previous attacks. In that case, 3 grains were given and the dose repeated in an hour. After the second dose this child was enabled to lie down and breathe with comfort. In one of the most severe cases the writer has ever seen the inhalation of nascent oxygen gave quick relief. This child was cyanotic, with cold, clammy skin, and short, panting breathing. The attacks came on without any preceding evidence of bronchitis. The oxygen was administered during three separate paroxysms, and always with prompt relief. In this particular case the attacks ceased at the age of five years and only recurred in a

¹ Osler's System, iii, 720.

lighter form at the age of eighteen years. At the time this patient was under my care a local druggist had an apparatus for the extemporaneous preparation of oxygen, so that it was possible to apply the remedy promptly.

In Osler's *System* the use of atropin hypodermically is recommended in doses sufficiently large to produce the physiological effect, but the writer has had personal experience with the remedy in only one case. The skin became flushed, but without marked relief.

There are cases in which after the severity of the paroxysm is relieved there remains a cough, with more or less wheezing and short breathing on exertion, that requires further attention. Here the use of heroin in a syrup of hypophosphites will often benefit by relieving the cough. In some cases in which the cough disturbs sleep, a single dose of antipyrin given at bedtime, will allay the cough and induce quiet sleep. The writer distinctly recalls 3 cases in which this remedy acted well after there had been no benefit from other drugs.

It is difficult to estimate the value of inhalations, but where there is a dry, teasing cough this treatment should be employed. The value of the treatment resides in the fact that the inhalation of moisture promotes expectoration. The use of a croup kettle is necessary, as it is neither possible nor best to saturate the room with steam. A number of remedies may be used in the steam. The writer prefers a combination of creosote and oil of eucalyptus, one teaspoonful of the mixture in a pint of water. The use of this combination with an improvised croup tent, for one-half hour at a time, and repeated two or three times in twenty-four hours, will often soften the cough and induce expectoration. Inhalations of lime water also will be of benefit.

Following the paroxysm of asthma, and until the cough is relieved, these children should receive very careful general care, including a restricted diet, attention to elimination, and careful regulation of the temperature and ventilation of the room, and proper covering to the body on going outdoors.

CONCLUSION. Basing my experience upon the study of the 20 cases mentioned in this paper, it is correct to affirm that the majority of infants and children suffering from asthma, ultimately recover. The writer has recently received reports from 10 cases that had been under his care in past years. In 8 cases there had been no return of asthma, and in the other 2 the paroxysms were lighter than in former years. The frequency and severity of the paroxysms can in a large measure be controlled by proper care and treatment. A limited number develop an emphysema, and as a result their general growth is permanently impaired. This is the most serious sequel of asthma, and because of this, all cases should receive prompt treatment, with a view of lessening

the severity and frequency of the paroxysms. The general care of asthmatic children is important, because in most cases a careful study will reveal some exciting cause that can be removed, or some morbid condition, as constipation or indicanuria, that can be corrected. Attention to these suggestions with diligence in discovering and removing other possible causes, will enable many asthmatic children to enjoy comparative freedom from attacks, and to develop into happy, useful citizens.

**THE TREATMENT OF FRACTURES OF THE FOREARM, WITH
NOTES OF THE END RESULTS OF 52 CASES
TREATED WITHOUT OPERATION.¹**

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NEARLY four years ago, in a paper discussing the end results of 61 cases of fracture of the femur, treated without operation, which was presented before this Academy,² it was stated that it seemed incumbent on those surgeons who advocated operative treatment as a matter of routine in cases of recent fracture "either to demonstrate the evil results which they regard as a necessary consequence of accepted" (that is, non-operative) "methods, or to bring forward proof that by operation still better results can be obtained, and without unjustifiable risk to the patient." It was further stated: "The advocates of operative treatment, in short, should either be able to show that the methods they propose will not increase the immediate mortality and will greatly diminish or altogether prevent the unfavorable results of conservative treatment; or, failing this, they should at least convince conservative surgeons that the functional results of the accepted forms of treatment are such as can no longer be tolerated."

To our knowledge no series of cases has been published, of fractures of any long bone in the body, demonstrating either the inadequacy of conservative measures or the superiority and equal safety of operative treatment. It is to show that a fairly large series of cases of fracture of the forearm, involving both bones

¹ Read before the Philadelphia Academy of Surgery, February 5, 1912.

² Ashhurst and Newell, *Annals of Surgery*, 1908, ii, 748.

in some part of their shafts, may be treated with satisfactory results without a single resort to operation, that we now present a study of these 52 cases. From this series are excluded cases of fractures involving the elbow or the wrist joint, and cases of Colles's fracture of the radius complicated by fracture of the ulnar styloid. Fractures of the forearm, thus limited to injuries of the shafts of the ulna and radius, do not form a large proportion of the cases of fracture seen, but they have been selected for this analysis because, next to those of the femur or leg bones, they are at present the type most often (and we believe usually quite unnecessarily) subjected to operation.

These patients were treated in the services of one of the writers at the Episcopal Hospital and at the Children's Hospital. In almost every case the patients first apply for treatment out of dispensary hours, soon after the accident which produced the fracture. They are dressed then by the surgical interne on duty in the receiving ward at the time, skiagraphs are made, and the patients are referred to the out-patient department for further treatment. Although in the very busy dispensary services in which they are treated it is not always practicable, our aim always has been to examine and dress with our own hands *all the recent fractures*, and to continue to dress them with our own hands *until union is fairly firm*. We have never relegated any cases of fracture to the care of orderlies or nurses, nor have we ever turned them over to the internes until we have ascertained by repeated and persistent personal instruction and supervision that the particular interne on duty was capable of applying the dressings in a satisfactory manner. In the treatment of fractures, as in many other important departments of surgery, one must remember that "eternal vigilance is the price of safety."

REDUCTION. "Reducing" a fracture is a relative term, since comparatively few broken bones can be accurately restored to their original form; and in the case of *shafts of long bones* it is not always necessary that reduction should be accurate. Nevertheless, the aim must be to secure as accurate reduction as possible, and in the case of fractures near joints (especially the elbow) accurate reduction is extremely important; but in the middle of the shaft of a long bone it is sufficient to secure *firm bony union*, with *no appreciable shortening*, and with *preservation of the normal axis of the limb*. For the first and second results to be obtained it is necessary for the fragments to be in contact "end-on," not only by lateral contact; and for the lateral displacement, not to exceed two-thirds of the diameter of the bone.

Anesthesia rarely will be necessary in reducing a fracture of the forearm if the surgeon takes advantage of the relaxation of the muscles which may be secured by position of the limb. *Full supination of the forearm* is the position preferred, with the elbow

flexed to a right angle. Correct replacement of the ulnar fracture usually can be determined clinically, as this bone is subcutaneous; but the radius is buried among so many muscles that a skiagraph frequently is necessary to ascertain the position of the fragments if the fracture is above the middle of the bone.

The forearm is then dressed *in full supination*³ between two straight splints, specially cut to fit each individual patient. They should be a little wider than the forearm, so as to prevent crowding the bones together laterally, but not so wide as to permit rotation of the forearm within the splints. The palmar splint extends from the bend of the elbow to the tips of the fingers, while the dorsal splint extends from the olecranon to the wrist. These splints should be smoothly but thickly padded with raw cotton. A longitudinal pad placed between the bones, in an effort to wedge them apart is not only useless but harmful. Extra compresses, however, may well be placed over any of the fragments that tend to project. The splints are then strapped snugly around the forearm by bands of adhesive plaster at the wrist and below the elbow, and are held securely in place by a roller bandage. A large "handkerchief" or "triangular" sling is applied, supporting the forearm throughout its length, and the forearm is carried against the chest, but always in full supination. In very small children, and in adults where the seat of fracture is near the elbow, this joint is immobilized by employing an anterior angular splint, known in Philadelphia as Hartshorne's, instead of the straight palmar splint.

The position of full supination is employed not only because supination is the most difficult part of rotation to regain,⁴ if once lost, and because the upper fragment of the radius usually is kept in supination by the biceps; but because it was found by one of the writers when the forearm was dressed in mid-pronation, as commonly advised now, and as formerly employed by him, that the fragments sagged by the force of gravity, and that the patients recovered not only with lost supination, but with angular deformity of both bones toward the ulnar side. If attempt is made to correct this deformity by adjusting a coaptation splint over the angular projection of the ulna, this may indeed be overcome, but the surgeon will succeed merely in forcing the ulna nearer the radius which cannot be influenced by such an appliance; and the dis-

³ According to Malgaigne (Fractures, Paris, 1847, p. 591) this position was condemned by Hippocrates, though used by his contemporaries. Its advantages were pointed out by Paré, who was opposed to the semi-prone position until he learned that the latter had been approved by Hippocrates, whereupon Paré resumed the use of the semiprone position. Malgaigne thought he was himself the first of modern surgeons to return to the use of full supination, advised in his *Anatomie Chirurgicale* (1838), until he learned that Lonsdale (London Med. Gaz., 1832, ix, 910) had preceded him.

⁴ The patient regains pronation by active use of the hand; very few motions require extreme supination.

ability as regards rotation will be increased. However, fractures in which no tendency to displacement exists, such as greenstick and subperiosteal fractures, may be treated successfully in the semi-prone position.

Often it is exceedingly difficult to keep these fractures even approximately reduced during the first week or ten days; and it is during this period that impatient surgeons are apt to urge operation as the only solution of the difficulty. But usually a little better position can be secured at each dressing, and when the ends of the bones begin to become sticky, during the second week, it will be found that deformity daily becomes less, and what looked at first (to the inexperienced) like a hopeless case, will result in a very useful arm, and one with slight or with no visible deformity. Skiagraphs are valuable and interesting, but a surgeon never should be terrified by the appearance of the forearm bones in a skiagraph into thinking that only operative treatment can give his patient a good result. If he uses the eyes in the ends of his fingers, he will secure by conservative means quite as good, and in many cases a much better result than by operation, and in a shorter time.

AFTER CARE. This involves removal of the dressing frequently enough to make sure that the soft parts are in good condition, and that reduction is maintained by the dressings employed. The surgeon never should neglect to see the patient on the day after the dressing is first applied, and to ascertain for himself that the limb is in good condition, and that the dressing is comfortable. An uncomfortable dressing always is inefficient, even if not positively harmful; but if the dressing is comfortable it is not desirable to redress the limb more than two or three times weekly at first, and less often as union progresses. As the splints and bandages are being removed for re-dressing, the patient sits facing the surgeon, and the forearm lies supine on the patient's thigh. The palmar splint is lifted carefully off without moving the forearm, and the flexor surface and sides of the forearm and hand are gently bathed in dilute alcohol; then without rotating the forearm at all it is gently raised as a whole from the dorsal splint, and the extensor surface is bathed similarly, correct apposition of the fragments being maintained all the time. Any undue haste or rapid movement or attempts at rotation will be painful, will evoke muscular spasm, and may cause displacement of the fragments.

We do not approve massage or mobilization in the treatment of fractures, except in so far as they are unavoidable in procuring proper care of the soft parts; and while we acknowledge the truth of the dictum of Lucas-Championnière that "a certain amount of motion between the fragments encourages the formation of callus," we are firmly of the opinion that even the most careful immobilization by splints allows, and proper care of the soft parts,

as above indicated, provides that "certain amount" of motion which is desirable; and that any surgeon who attempts more, in the vain idea that he is following modern teaching, will succeed either in stirring up such an amount of callus (especially in children) as to cause deformity and injurious pressure on the soft parts, or (in most adults) will leave his patient with an ununited fracture.

When the ends of the bones become "sticky" and no tendency to displacement exists, the surgeon may then begin to make very limited degrees of passive motion in the neighboring joints at each dressing, meanwhile maintaining support at the seat of fracture. Under no circumstances should the passive motion cause pain. When union is firm enough for all external support to be discontinued, function usually will be more comfortably and quickly recovered by active movements by the patient himself, than by further attempts at passive motion; and if a fracture has been treated properly in the first place, massage very rarely will be necessary to accelerate the cure.

OPERATIVE TREATMENT OF SIMPLE FRACTURES. We believe there are only two indications for the "open method" of treating simple fractures: (1) If the fracture cannot be properly reduced without operation, and (2) if proper reduction cannot be maintained without direct fixation of the fragments.

1. *When Proper Reduction is Impossible.* Impossibility is here a relative term, since what is impossible for one surgeon may not be so for another; and the qualification "proper" reduction is employed because we do not wish to imply that operation is indicated whenever accurate, exact, perfect, anatomical replacement is impossible, but only when such degree of reduction, as has been described in a previous paragraph as requisite for proper function, cannot be secured without open operation. Less perfect reduction is requisite in children than in adults, since in the former compensation is more rapidly established; and oblique fractures require less close and accurate apposition of their ends than do transverse fractures.

2. *When Subsequent Displacement Cannot be Prevented.* This also is a relative condition, depending on the skill of the surgeon in devising and applying efficient retentive apparatus, and upon the extent to which displacement occurs.

After operation the process of union often is slower than it would have been if no operation had been employed; and in a fair proportion of cases operated on by the average surgeon a mild degree of infection occurs, and only fibrous union results.

STATISTICS. These cases form a continuous series, absolutely unselected, running through a period of ten years. Of 66 patients treated, the end results are known in 52 cases; 43 of the fractures occurred in males, and only 9 in females. None of the female patients was older than fifteen years. Of the males, 31 were less

than fifteen years of age, and 12 were older. The youngest patient (a girl) was seventeen months old, and the oldest (a man) was fifty-seven years. The right and left arms were affected nearly with equal frequency.

For estimating the power of rotation, a special instrument (Fig. 1) was devised, and was constructed for us by D. W. Kolbe Co. For establishing a standard, the average normal rotation was ascertained by testing one hundred normal forearms of fifty persons (25 male, 25 female). The instrument consists of an indicator, kept vertical by gravity, and centred on a circular protractor. This protractor is attached to an upright board which itself is

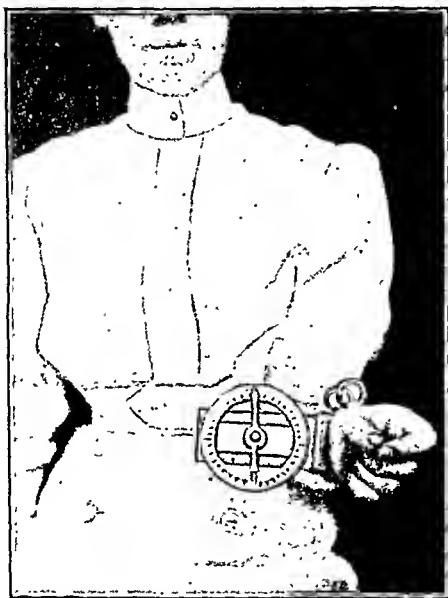


FIG. 1.—Pronometer, or instrument for measuring the degree of pronation and supination. Indicator points to zero degrees in supine position.

fastened at right angles to a horizontal board. The horizontal board is strapped on the flexor surface of the wrist, the forearm being in full supination. In this position the indicator points to 0 degrees. If still further supination is possible, this is recorded as a *minus* quantity, of say 5, 10, or 15 degrees. As the forearm is rotated into pronation the protractor also rotates, but the indicator remains vertical and passes over the rotating scale from 0 degree up to 135 degrees or 140 degrees or more, according to the extent of pronation possible (Fig. 2). During this examination, it is needless to say, the patient's humerus should be kept immovably applied to the side of the thorax, and no deviation of the body from the vertical should be permitted.

NORMAL ROTATION. Our examination of 100 normal forearms gave the following results:

Ages varied from fourteen to seventy-seven years; average age, twenty-nine years.

Supination: Greatest . . . —45.00 degrees. Least 15.00 degrees.
 Average . . . —11.72 degrees. { In males — 7.42 degrees.
 Average of right forearm —7.24 degrees; of left —16.2 degrees. { In females. . . . —16.02 degrees.

Pronation: Greatest 180.00 degrees. Least 120.00 degrees.
 Average 147.77 degrees. { In males 148.24 degrees.
 Average of right forearm, 147.24 degrees; of left, 148.00 degrees. { In females 147.30 degrees.

Greatest range of rotation in any one patient, from —45 degrees to 155 degrees, or 200 degrees.
 Least range of rotation in any one patient from 0 degree to 122 degrees, or 122 degrees.
 Average rotation from —11.72 degrees to 147.77 degrees, or 159.49 degrees.



FIG. 2.—Pronometer. Indicator points to 90 degrees when forearm is in "mid-pronation."

RESULTS. In studying the end results of these 52 cases, it may first be stated what was not secured: there was no case of gangrene of the soft parts or of necrosis of the bones; there was no case of ischemic contracture; none of nerve lesion; none of ununited fracture; none of conspicuous deformity. There was one case of delayed union (Case 37), but this patient cured himself, by returning to his work as a blacksmith at the end of ten weeks. There were several cases in which some thickening or irregularity could be felt at the site of fracture; but none in which these were appreciable at a glance. There was no case of disability, even slight. And these results were obtained without excluding 9 more or less complicated cases, as follows: 1 case of badly comminuted fracture (Case 39); 1 case of fracture of both bones of both forearms (Cases 2 and 3); 3 cases of multiple fractures of the upper extremity (Cases 1, 25, 26) involving both the humerus and the bones of

the forearm, two of which were compound comminuted fractures; as well as 3 other cases of compound fracture (Cases 7, 32, 47). None of the cases of compound fracture, however, was such as to require operation on account of the condition of the soft parts.

The end results may be seen at a glance in the following table. Under the heading "perfect result" we include only such cases as have recovered without palpable deformity, and with preservation of perfect function. If, in spite of preservation of perfect function, there is palpable deformity, as in Cases 2 and 3, the patients are recorded in the second column, as "slight deformity, but perfect function." If there is limitation of function the cases are placed in the third column; in none was there any limitation of function except in rotation; and in none was there any disability.

END RESULTS OF FIFTY-TWO CASES OF FRACTURE OF BOTH BONES OF THE FOREARM.

Character of fracture.	Class I.	Class II.	Class III.
	Perfect result.	Slight deformity.	Rotation limited.
Greenstick	10	1	0
Simple complete	22	8	4
Simple comminuted	0	0	1
Compound	1	1	1
Compound comminuted	1	0	2
Total	34 (65.4%)	10 (19.2%)	8 (15.4%)

The skiagraphs of end results, which we have chosen for reproduction here, are those of cases in which the prognosis seemed least favorable, and represent, therefore, much worse than the average skiagraphic results. As far as cosmetic results are concerned, there was no visible deformity in any of these cases except in Cases 2, 3, 26, 39, 48, and 51; and in these patients a mere glance at the bared arm will not detect any deformity.

In Class I we have included Cases 1, 4, 5, 6, 8, 10, 11, 12, 14, 16, 17, 18, 19, 22, 23, 24, 25, 27, 28, 29, 31, 34, 35, 36, 37, 38, 41, 42, 43, 44, 45, 46, 50, 52.

In Class II are included Cases 2, 3, 20, 21, 30, 33, 40, 47, 48, 49.

In Class III are included Cases 7, 9, 13, 15, 26, 32, 39, 51.

We are greatly indebted to Dr. Thos. S. Stewart, radiographer to the Episcopal Hospital, and to his assistant, Dr. A. R. W. Wilkinson, for the interest they have taken in providing us with numerous skiagraphs for the purpose of this study.

ABSTRACTS OF CASE HISTORIES.

CASE 1.—Michael C., aged fifteen years. May 6, 1902. Episcopal Hospital. Multiple fractures of right upper extremity (surgical neck of humerus, both bones of forearm, compound of ulna). Recorded as Case I in a paper on "Multiple Fractures" (Ashhurst,

Annals of Surgery, 1907, ii, 263). Full supination. Examined February 20, 1907. No visible or palpable deformity anywhere. Does heavy laboring work, and would not know arm ever had been injured. Perfect result. Class I. (Fig. 3.)



FIG. 3.—Case I. Five years after compound fracture of both bones of forearm, and fracture of humerus. No deformity. Perfect function.

CASES 2 and 3.—Augustus F., aged thirty-five years. March 16, 1903. Episcopal Hospital. Fracture of both bones of both forearms, sixteen days previously; has been dressed on internal angular and short dorsal splints, in position of mid-pronation. Arms gave constant pain. No attempt at union, because fragments were not in contact and were not immobilized. By putting forearms in full supination better position was secured, but complete reduction was impossible. However, pain was immediately and absolutely relieved. Two weeks later, good union. Examined October 28, 1911. Says he never knows arms were broken; was out of work only fourteen weeks in all, and has worked as machinist ever since with perfect function. There is no visible deformity, but the displaced fragments are still palpable. Supination in both forearms complete; pronation on right to 135 degrees, and on left to 130 degrees. Without seeing the skiagraphs made recently (Figs. 4 and 5), the results might be considered perfect. Class II.

CASE 4.—Harry H., aged ten years. September 1, 1903. Episcopal Hospital. Right. Treated in supination. Examined October 28, 1911. Full supination, pronation to 165. Class I.

CASE 5.—Phoebe G., aged two years. October 15, 1903. Episcopal Hospital. Right, greenstick. Examined October 28, 1911. Full supination, pronation to 160. Class I.

CASE 6.—Adolph W., aged ten years. October 19, 1903. Episcopal Hospital. Right. Examined, January 28, 1912. Broken

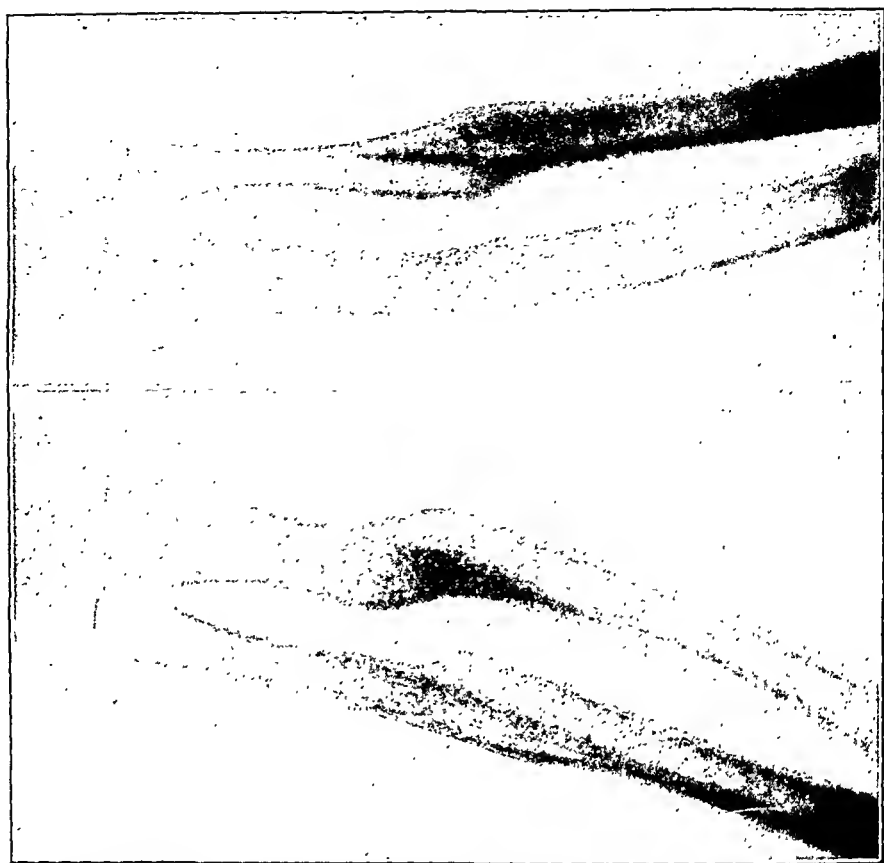


FIG. 4.—Cases II and III. Antero-posterior views of both forearms, eight years after injury. Function perfect.

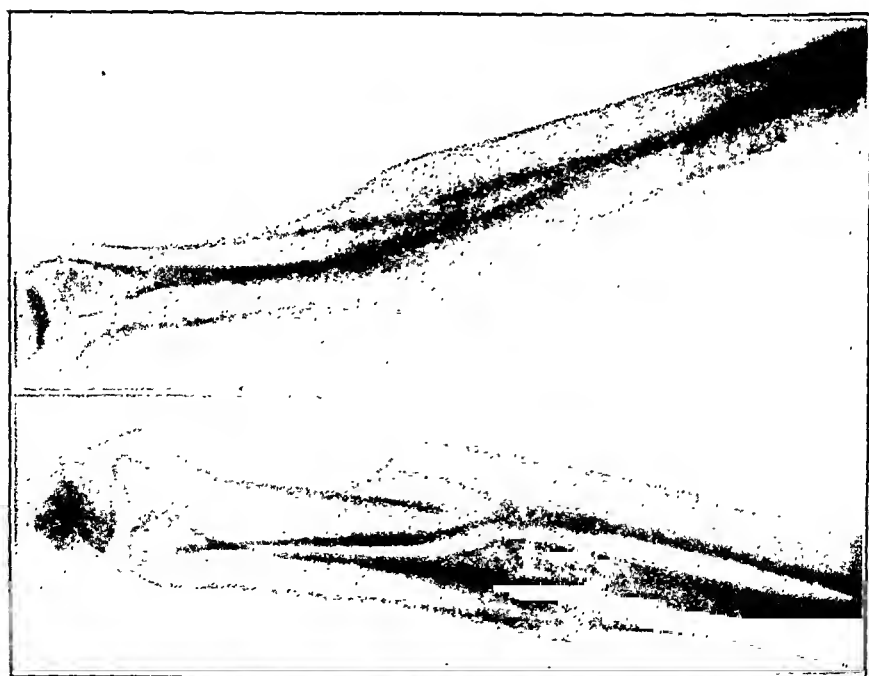


FIG. 5.—Cases II and III. Lateral view of both forearms eight years after injury. Function perfect. Patient first came under the writer's care sixteen days after injury.

arm, supination —20 degrees, pronation 130 degrees; normal arm, supination —15 degrees, pronation 135 degrees. Class I.

CASE 7.—William T. S., aged forty years. January 18, 1904. Episcopal Hospital. Right, simple of radius, compound comminuted of ulna. Examined five weeks later. Function good, but some limitation of supination. Class III.

CASE 8.—Fred. S., aged fifteen years. January 18, 1904. Episcopal Hospital. Dressed in full supination. Examined March, 1904. Class I.

CASE 9.—Thomas M., aged twenty-five years. January 19, 1904. Episcopal Hospital. Left, above middle. Great and persistent overlapping, with projection of upper fragments of radius and ulna on extensor surface. Dressed in mid-pronation, on internal angular and short dorsal splint. Examined March 12, 1904. Very slight deformity; no supination beyond mid-position. Class III.

CASE 10.—George H., aged twenty-eight years. January 23, 1904. Episcopal Hospital. Left, middle third. Dressed in mid-pronation. Examined, March 12, 1904. Class I.

CASE 11.—Emma L., aged two years. January 31, 1904. Episcopal Hospital. Greenstick. Examined March 3, 1904. Class I.

CASE 12.—William A., aged twelve years. April 12, 1904. Episcopal Hospital. Left, treated in mid-pronation. Examined October 28, 1911. Supination full, pronation to 135 degrees. Class I.

CASE 13.—Fred. H., aged sixteen years. April 15, 1904. Episcopal Hospital. Right, dressed in mid-pronation. Had refracture of same forearm in November, 1904. Examined January 27, 1912. No deformity, no disability. Right: supination, 25 degrees; pronation, 120 degrees. Left: supination, 20 degrees; pronation, 145 degrees. Class III.

CASE 14.—Albert S., aged thirteen years. September 1, 1904. Episcopal Hospital. Greenstick. Treated in mid-pronation. Examined October, 1904. Class I.

CASE 15.—James M., aged eight years. September 8, 1904. Episcopal Hospital. Left lower third. Very great cellulitis. Treated in mid-pronation. Examined October, 1904. No deformity, but little supination beyond mid-position. Class III.

CASE 16.—Thomas McG., aged fourteen years. December 7, 1905. Episcopal Hospital. Right; of radius above insertion of pronator teres, and greenstick of ulna, same level. Treated in full supination. Examined December 29, 1905. No deformity, full supination, pronation good. Class I.

CASE 17.—Anna D., aged fourteen years. December 23, 1905. Episcopal Hospital. Right. Treated in full supination. Examined January 15, 1906. Class I.

CASE 18.—John F., aged thirteen years. December 29, 1905. Episcopal Hospital. Middle third. Treated in full supination.

Examined October 28, 1911. Full supination, pronation 165 degrees. Class I.

CASE 19.—Juliette J., aged eight years. July 3, 1906. Children's Hospital. Greenstick, middle third. Treated in full supination. Examined August 2, 1906. Class I.

CASE 20.—Carrie C., aged six years. August 2, 1906. Children's Hospital. Injury two weeks ago at Atlantic City, and dressed in mid-pronation. On admission today, fracture at junction of middle and lower thirds of right forearm; no union, fair position; but bowing of ulna to extensor surface. Treated in full supination. August 21, union good, no deformity; full supination and pronation. Examined August 28, 1906. Upper fragment of ulna displaced slightly posteriorly; functions perfect. Class II.

CASE 21.—John S., aged twelve years. August 6, 1906. Children's Hospital. Left, junction of middle and lower thirds. Fell from tree; was stunned. Upper fragment of ulna projects beneath skin of flexor surface; both lower fragments displaced toward extensor and radial surfaces. Treated in full supination. August 10. Deformity persists; pad over upper fragment of ulna. August 14. Position better; growing firmer. August 21. Position fair; bones firm. Examined September 5, 1906. Little deformity, no disability; supination and pronation complete. Class II.

CASE 22.—William G., aged seven years. November 3, 1906. Episcopal Hospital. Left, greenstick, middle third. Dressed in full supination. Then patient visited another dispensary, and when splint applied there fell off of itself, he returned to Episcopal Hospital, November 19, with marked dorsal bowing of both bones. Bones were re-fractured, deformity reduced, and forearm dressed in full supination. Examined December 10, 1906. No visible deformity, but a little callus palpable over radius. Full supination and pronation. Class I.

CASE 23.—Albert S., aged eleven years. November 15, 1906. Episcopal Hospital. Right, complete of radius, greenstick of ulna. Dressed in full supination. Examined December 12, 1906. Class I.

CASE 24.—Hugh F., aged fourteen years. November 21, 1906. Episcopal Hospital. Left, above wrist. Full supination. Examined October 28, 1911. Supination complete, pronation to 180 degrees. Class I.

CASE 25.—Andrew M., aged fourteen years. December 22, 1906. Episcopal Hospital. Left; compound comminuted fracture of both bones of left forearm with compound comminuted fracture of left humerus. (Reported as Case VI in paper on "Multiple Fractures," in *Annals of Surgery*, 1907, ii, 263.) Treated in ward for nine days, then in dispensary. Forearm dressed in full supination. Fig. 6 is from a photograph taken three months after the accident. Examined October 28, 1911. Supination and pronation

complete. No deformity. Figs. 7 and 8 are from skiagraphs made in January, 1912. Class I.



FIG. 6.—Case XXV. Compound comminuted fractures of both bones of left forearm, with compound comminuted fracture of left humerus. No deformity. Perfect function. See Figs. 7 and 8.

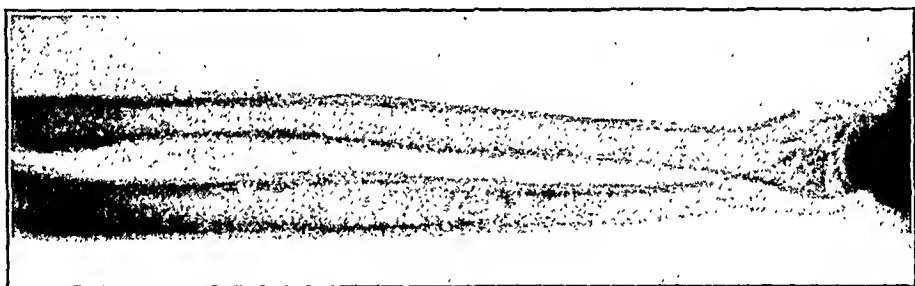


FIG. 7.—Case XXV. Lateral view of forearm five years after compound comminuted fracture of both bones.

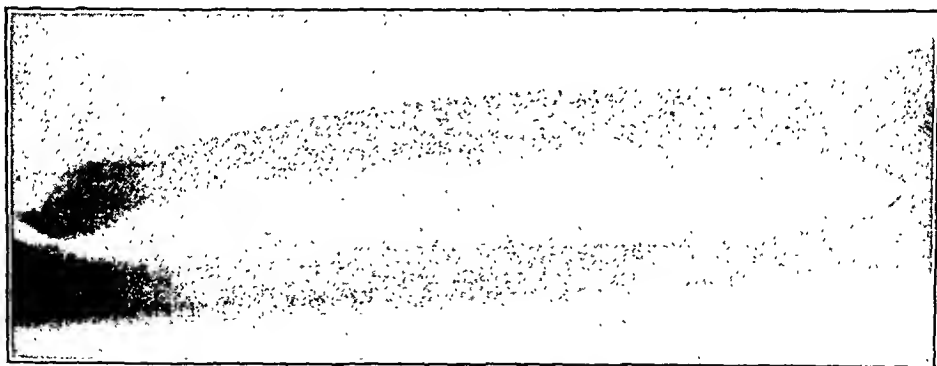


FIG. 8.—Case XXV. Antero-posterior view of forearm, five years after compound comminuted fracture of both bones.

CASE 26.—Henry D. E., aged fifty-seven years. November 26, 1906. Episcopal Hospital. Left. Compound comminuted fracture of both bones of left forearm, with comminuted fracture of left humerus. (Reported as Case V, in paper on "Multiple Fractures," in *Annals of Surgery*, 1907, ii, 263.) Treated with

forearm in full supination. Examined January 21, 1912. Was out of work (saw-maker) for four months. Complete function not regained for one year. Since then has experienced no disability whatever. There is considerable deformity in forearm, bones being bowed to radial side. Left forearm: supination, 0 degrees; pronation, to 85 degrees. Right forearm: supination, 0 degrees; pronation, to 155 degrees. Class III.

CASE 27.—Albert B., aged three years. March 5, 1907. Episcopal Hospital. Right, greenstick, two weeks old; bones bowed to extensor surface, some callus; inability to supinate completely. Refractured, and dressed in full supination. Examined April 4, 1907. No deformity, supination and pronation complete. Class I.

CASE 28.—Harriet B., aged two years. March 29, 1907. Episcopal Hospital. Left, greenstick. Full supination. Examined April 26, 1907. Supination and pronation complete. Class I.

CASE 29.—Charles G., aged fourteen years. January 9, 1908. Episcopal Hospital. Left, full supination. Examined February 13, 1908. Class I.

CASE 30.—Harry W., aged thirty months. July 8, 1907. Children's Hospital. Left, greenstick. One month's duration. Very marked angulation just above wrist, about 135 degrees, angle being open on extensor surface. Refractured (ether) and dressed in full supination. July 15, no union yet. July 20, some union. Examined, August 15, 1907. Slight radial deviation of hand, due to rachitic deformity, same as in other arm. Supination and pronation complete. Class II.

CASE 31.—George W. D., aged fourteen years. July 23, 1907. Children's Hospital. Right, lower third. Full supination. Examined August 29, 1907. Supination complete, pronation about 140 degrees. Class I.

CASE 32.—Dillman F., aged five years. June 21, 1907. Children's Hospital. Right; compound of ulna. Dressed in mid-pronation. Examined August 8, 1907. Supination not quite complete, pronation complete. Some callus over radius, and slight deformity to flexor surface. Functions perfect. Class III.

CASE 33.—Clark W. B., aged four years. July 29, 1907. Children's Hospital. Left; same forearm was broken two years ago. Dressed in full supination. Examined August 29, 1907. Both bones bowed slightly to radial aspect; rotation from full supination is good. Class II.

CASE 34.—John H., aged twenty-two months. January 13, 1908. Episcopal Hospital. Left, greenstick. Full supination. Examined February, 1908. Class I.

CASE 35.—Marcus D., aged sixteen years. April 14, 1908. Episcopal Hospital. Epiphyseal separation of radius and greenstick of ulna above styloid. Full supination. Examined October 28, 1911. Class I.

CASE 36.—Louis S., aged fourteen years. April 22, 1908. Episcopal Hospital. Left, lower fifth. Full supination. Examined June 2, 1908. Class I.

CASE 37.—Charles W. H., aged 18 months. January 4, 1909. Episcopal Hospital. Left, greenstick. Full supination. Examined March, 1909. Class I.

CASE 38.—Clara Y., aged nine years. February 10, 1909. Episcopal Hospital. Right, two inches above wrist. Dressed on Bond splint, in mid-pronation, there being no tendency to deformity. Examined October 28, 1911. Class I.

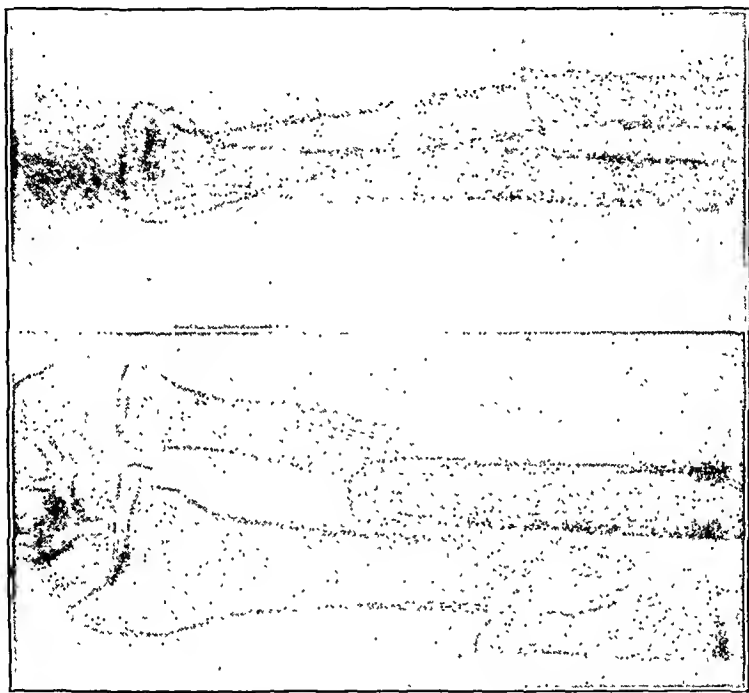


FIG. 9.—Case XXXIX. Lateral and antero-posterior views of comminuted fracture of both bones of forearm, showing best position secured. See Fig. 10.

CASE 39.—Michael S., aged fifty-three years. February 25, 1909. Episcopal Hospital. Right; comminuted; was caught in machinery. Dressed in full supination; accurate reduction not secured (Fig. 9). Delayed union. After ten weeks returned to his work (blacksmith), and two months later had firm union. Examined January 20, 1912. Right forearm: supination, 15 degrees; pronation, 105 degrees. Left forearm: supination, 0 degrees; pronation, 140 degrees. There is slight palpable bony deformity, but no disability whatever (Fig. 10). Class III.

CASE 40.—Victoria K., aged seventeen months. February 16, 1910. Episcopal Hospital. Right. Dressed in mid-pronation. Examined ten weeks later. Slight extensor bowing of ulna; supination and pronation complete. Class II.

CASE 41.—Wilson McC., aged fourteen years. March 23, 1910. Episcopal Hospital. Right, lower third. Full supination. Examined, January 20, 1912. No deformity palpable. Right forearm: supination, —35 degrees; pronation, 125 degrees. Left forearm: supination, —40 degrees; pronation, 140 degrees. Class I.

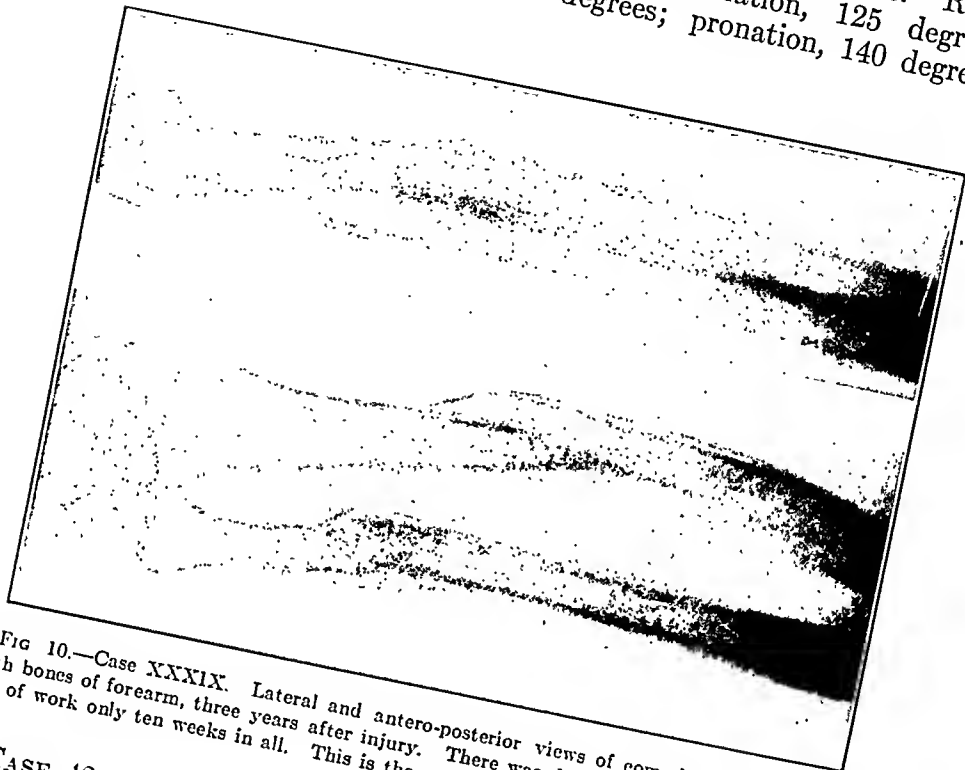


FIG 10.—Case XXXIX. Lateral and antero-posterior views of comminuted fracture of both bones of forearm, three years after injury. There was delayed union, but patient was out of work only ten weeks in all. This is the worst result in the entire series.

CASE 42.—William E., aged fifteen years. January 18, 1911. Episcopal Hospital. Right, above wrist. Full supination. Examined October 28, 1911. Class I.

CASE 43.—Helen K., aged three years. January 28, 1911. Episcopal Hospital. Right, greenstick. Full supination. Examined October 28, 1911. Supination complete, pronation to 170 degrees. Class I.

CASE 44.—John L., aged seventeen years. August 11, 1911. Episcopal Hospital. Complete of radius, greenstick of ulna. Full supination. Examined October 28, 1911. Perfect result. Supination complete, pronation to 160 degrees. Class I.

CASE 45.—George S., aged nine years. August 11, 1911. Episcopal Hospital. Middle third, left; has been dressed in mid-pronation at another hospital. Examined October 27, 1911. Supination complete, pronation to 135 degrees. Class I.

CASE 46.—Harry M., aged thirteen years. August 16, 1911. Episcopal Hospital. Right, above wrist. Full supination. Ex-

amed October 28, 1911. Supination complete, pronation to 135 degrees. Class I.

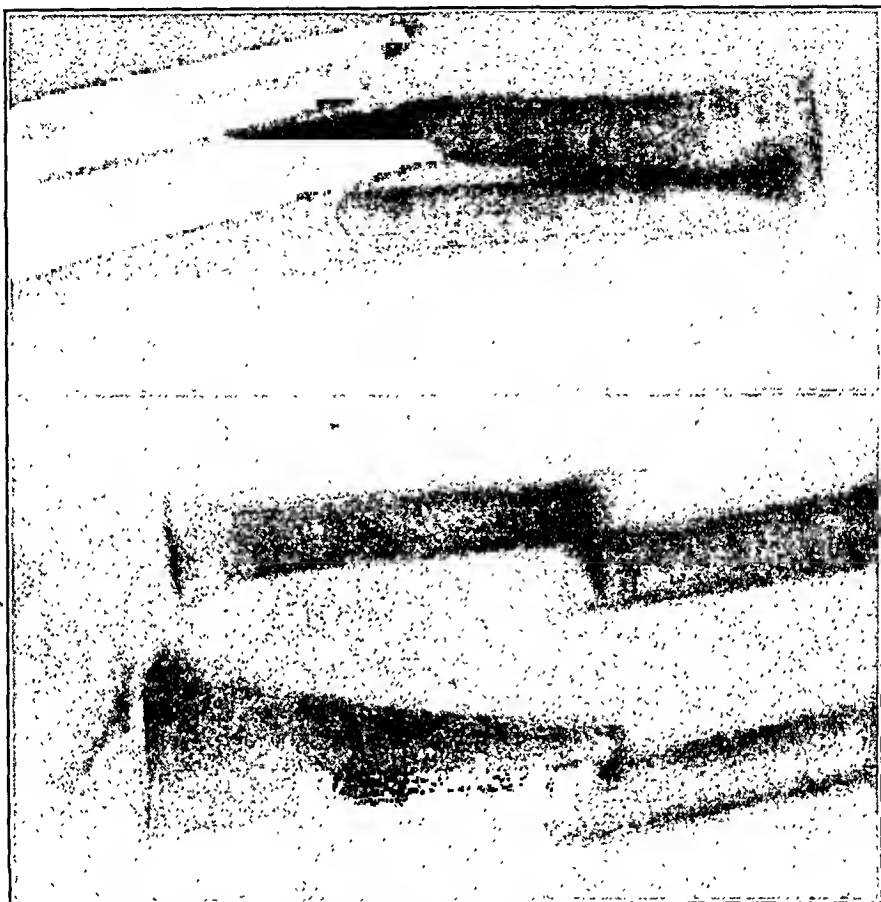


FIG. 11.—Case XLVII. Compound fracture of radius and ulna, before coming under care of the writers, and while still dressed in mid-pronation. See Figs. 12 and 13.

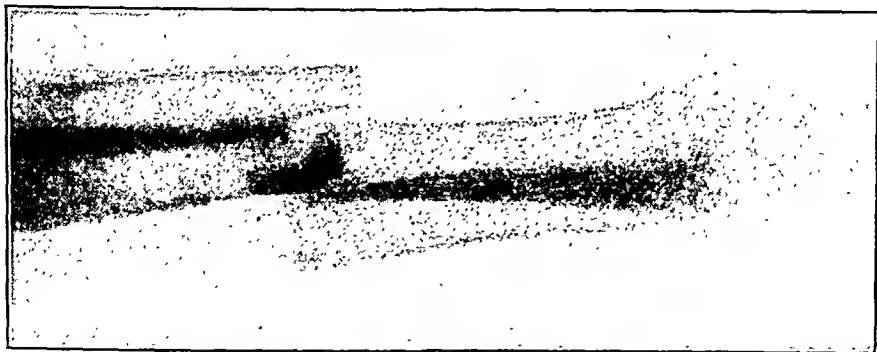


FIG. 12.—Case XLVII. Lateral view, after dressing in full supination, one week after injury.

CASE 47.—Roger McB., aged nine years. August 17, 1911. Episcopal Hospital. Injury one week ago, and was referred as suitable for operation; had been dressed in mid-pronation (Fig. 11).

Better position secured by dressing in full supination (Figs. 12 and 13), and no operation recommended. Compound fracture of radius and ulna, wounds on flexor surface of forearm. Examined January 20, 1912. Slight amount of callus palpable. Injured forearm: supination, -30 degrees; pronation, 130 degrees. Normal forearm: supination, -20 degrees; pronation, 135 degrees. Class II. (Fig. 14.)



FIG. 13.—Case XLVII. Antero-posterior view after dressing in full supination.

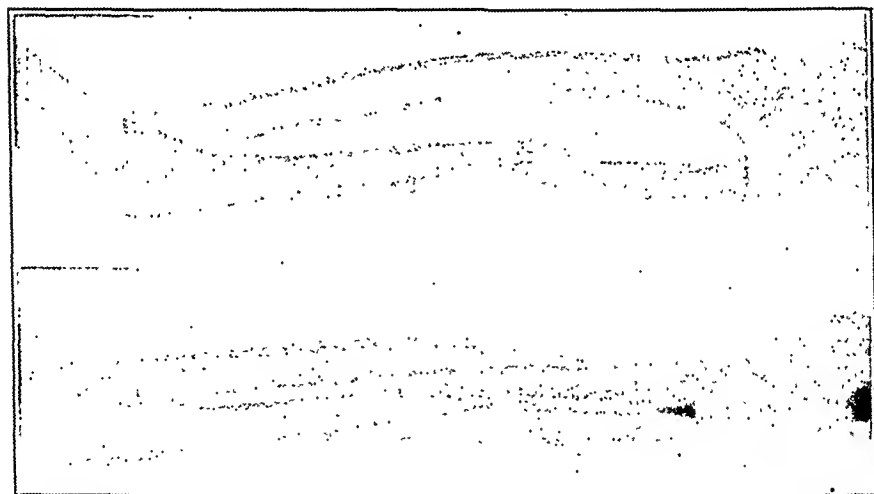


FIG. 14.—Case XLVII. Compound fracture of both bones of forearm five months after injury. Slight callus palpable. No visible deformity. Perfect function.

CASE 48.—Tony M., aged fourteen years. September 8, 1911. Episcopal Hospital. Left; injury one week ago, junction of middle and upper thirds. Had been dressed in mid-pronation. Better position secured by dressing in full supination. Examined January 21, 1912. Slight posterior bowing of both bones. Left forearm: supination, 20 degrees; pronation, 150 degrees. Right

forearm: supination, -5 degrees; pronation, 140 degrees. Class II.

CASE 49.—Richard W., aged thirteen years. September 23, 1911. Episcopal Hospital. Left, middle third. Full supination. Skiagraph (Fig. 15) showed lower fragment of radius displaced

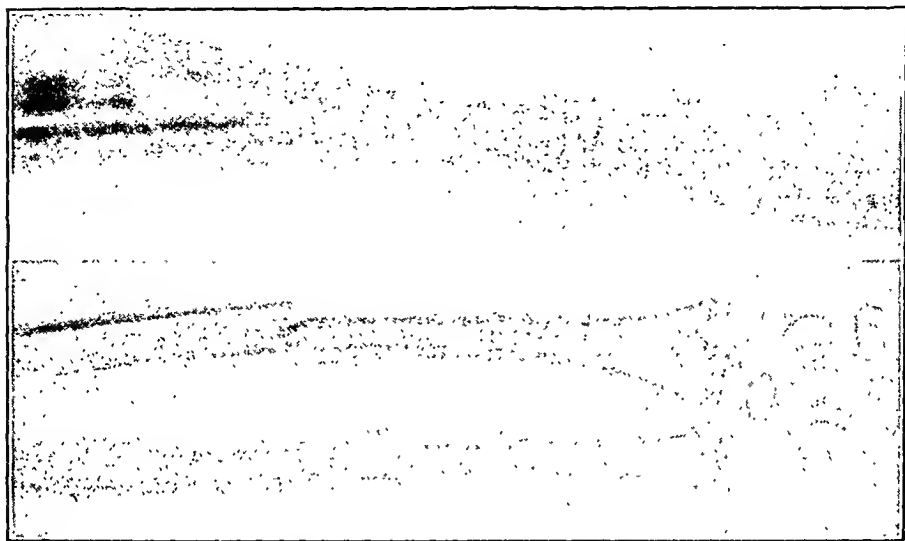


FIG. 15.—Case XLIX. Lateral and antero-posterior views after first dressing. See Fig. 16.

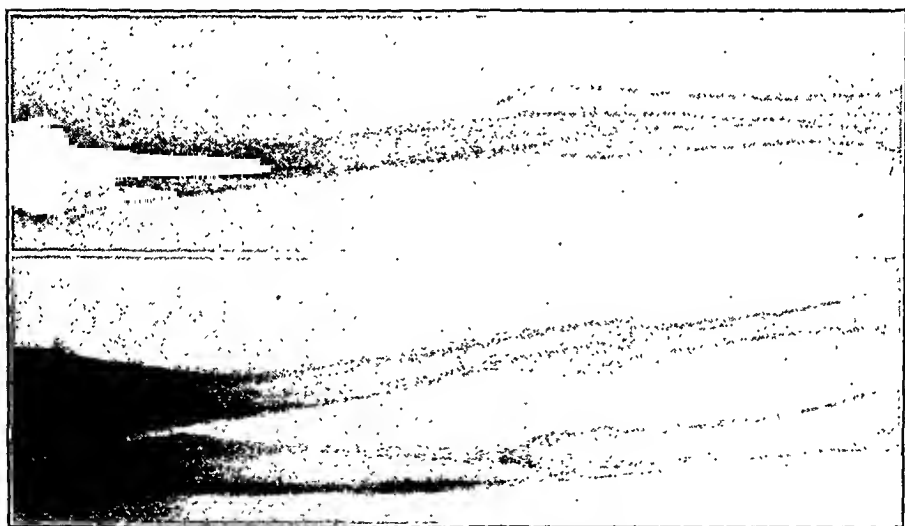


FIG. 16.—Case XLIX. Lateral and antero-posterior views four months after injury. Slight callus palpable. No visible deformity. Perfect function.

to flexor surface. Examined, January 17, 1912. No visible deformity, slight callus palpable on flexor surface of radius (Fig. 16). Left forearm: supination, -15 degrees; pronation, 125 degrees. Right forearm: supination, -10 degrees; pronation, 135 degrees. Class II.

CASE 50.—Herbert T., aged fourteen years. September 26, 1911. Episcopal Hospital. Right, middle third. Dressed in full supination. Examined January 21, 1912. Some callus palpable. Right forearm: supination, —10 degrees; pronation, 155 degrees. Left forearm: supination, —10 degrees; pronation, 140 degrees. Class I.

CASE 51.—John D., aged eighteen years. October 10, 1911. Episcopal Hospital. Right, junction of middle and upper third. Full supination. Some projection of upper fragment of radius on flexor surface. Examined January 28, 1912. Slight callus of radius. Right forearm: supination, 40 degrees; pronation, 135 degrees. Left forearm: supination, —5 degrees; pronation, 120 degrees. Class III. (This patient was under the care of the writers only seventeen days.)

CASE 52.—Stanley C., aged fourteen years. October 10, 1911. Episcopal Hospital. Left, lower third of radius, and through lower epiphysis of ulna. Full supination. Examined January 27, 1912. Left forearm: supination —15 degrees; pronation, 160 degrees. Right forearm: supination, —5 degrees; pronation, 160 degrees. Class I.

FURTHER EVIDENCE IN SUPPORT OF THE TOXIC PATHOGENESIS OF BRONCHIAL ASTHMA, BASED UPON EXPERIMENTAL RESEARCH.

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IN 1905, in a paper before the Orleans Parish Medical Society,¹ I called the attention of the profession to the importance of a consideration of the role played by intestinal toxins in producing various pathological conditions. Since then I have given the matter special attention, and I had already collected several cases of bronchial asthma, associated with intestinal toxins, which were relieved by abolishing the intestinal toxemia, when Rochester² read his paper in 1906, before the Section on Medicine of the American Medical Association. The discussion following this paper showed that the general opinion of the profession was opposed

¹ Proceedings Orleans Parish Medical Society, 1905.

² Jour. Amer. Med. Assoc., 1906, xlvii, 1933.

to the toxic pathogenesis of asthma. In 1909, before the Louisiana State Medical Society,³ I reported several cases of bronchial asthma relieved entirely along dietetic lines by relieving the associated toxemia of intestinal origin; but discussion by Dock and others again revealed the fact that the profession was not as yet prepared to accept the toxemic basis of this symptom.

Since first becoming interested in the subject, I have collected histories of 121 cases of spasmodic bronchial asthma, partly my own and partly from other clinicians, which were associated with an intestinal toxemia, and were relieved by relieving this latter condition.

While I am not prepared, as yet, to claim that every case of asthma is due to a special toxin of intestinal origin and produced by the putrefaction of proteid material, I have yet to see one case in which, in my opinion, it is not the underlying cause.

Bouchard,⁴ nearly twenty years ago, in speaking of paroxysmal attacks of asthma, states: "These, also, I suspect, we must rather consider the result of the elimination of toxic substances than a reflex act." However, in reading the literature pertaining to this so-called disease, one is struck by the various hypotheses expounded as to its etiology. Saenger⁵ believes the underlying cause is an inherited "neurosis," with a mechanical obstruction superinduced by bronchial catarrh, and his treatment consists in relieving the latter condition by inhalations, etc.

Goldschmidt⁶ also presupposes an hereditary neurosis, and classifies asthma into: (1) "Ein asthma epilepticum s. nervosum; (2) ein asthma bronchiale s. catarrhale paroxysmale; (3) ein asthma catarrhale chronicum; (4) ein asthma catarrhale permanens."

However, he recognizes: (1) "Ein asthma toxicum (aetiologische); (2) ein asthma catarrhale (anatomische); (3) ein asthma reflexivum (physiologische)."

He considers that the disease can best be classified according to its associated symptomatology, but in his toxic type he apparently considers that carbon dioxide poisoning of the blood stimulates the respiratory centre, resulting in the bronchial spasm, and does not mention the likelihood of intestinal toxins playing any important role. This view, to me, is untenable, after reviewing the recent work on the physiology of the respiratory centre carried on by Henderson⁷ and others.

Bergmann⁸ classifies asthma into: (1) A traumatic asthma, caused by stimulation of the respiratory centre through trauma to the cerebrum or medulla, as well as through a psychical defect

³ Proceedings Louisiana State Medical Society, 1909.

⁴ Lectures on Auto-intoxication in Disease, 1894, p. 171.

⁵ Ueber Asthma und seine Behandlung, Berlin, 1910.

⁶ Asthma, Munich, 1910.

⁷ Johns Hopkins Hosp. Bull., xxi, 1910, 233.

⁸ Das Asthma, sein Wesen und sein Behandlung, Wiesbaden, 1910, p. 36.

(2) A reflex asthma, caused by stimulation of the respiratory centre, through abnormalities in the various mucous membranes, as well as through a reflex stimulation of the respiratory centre through the central organism itself, as in so-called neurasthenia. (3) A toxic asthma, caused by the stimulation of the respiratory centre through the toxic condition of the blood.

Many other classifications are proposed, such as teeth asthma, supposed to be caused by defective teeth; dyspeptic asthma; and sexual asthma, especially advocated by Sadger,⁹ a pupil of Freud.

The various classifications will continue to grow as long as we regard asthma as a distinct disease, instead of as a symptom of some other underlying constitutional condition.

The few reports of postmortem sections of patients dying in attacks of asthma, which I have been able to find in the literature,¹⁰ are so widely at variance that no definite idea can be formed as to the pathology of this condition, further pointing to the fact that asthma should be classified as a symptom of an underlying constitutional pathological condition, associated sometimes with epilepsy, sometimes with cardiac disease, and at times, probably, with every disease known.

Hare¹¹ lays a great deal of stress upon the toxic basis of asthma, but his conclusions that it is brought on by "glycogenic distention of the liver," with resulting hypocarbonization of carbohydrates, is not based upon sound physiological facts, nor are his results in accord with my experience. More likely the engorgement of the liver of which he speaks allows the intestinal toxins to pass through into the general circulation without being synthesized, and their toxic action is thus manifested.

During the past summer and autumn, while working in Vienna with Prof. Karl von Noorden and Prof. Richard Kraus, I decided to attempt to prove or disprove our clinical deductions by animal gentlemen experimentation, and I wish to take this means of thanking these for their courtesy and assistance during my investigations and for their free provision of material.

The hypothesis put forward to prove was: "If asthma is caused by intestinal toxemia a definite toxin exists, which causes bronchial spasm similar in action to muscarin, and this toxin originates in the intestinal canal." In seeking this specific toxin, I was led to investigate theamins formed by intestinal putrefaction of the several amino-acids of normal pancreatic digestion of proteids, as I had long since satisfied myself by earlier chemical investigation and from the work of others, that the Charcot-Leyden crystals

⁹ Zentralbl. f. Psychoanalyse, 1911, Hefte 5 and 6, p. 200.

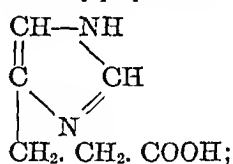
¹⁰ Meeting held by the Militärärztlichen Gesellschaft, Berlin, 1886, p. 13; also see Berkast on Bronchial Asthma, its Pathology and Treatment, London, 1887; and Proceedings of the London Pathological Society, 1903.

¹¹ The Food Factor in Disease, London, 1905.

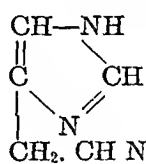
are amins closely allied to putrescin and cadaverin. On putrefaction the several amino-acids split off carbon dioxide and form their corresponding amins; so that we find a corresponding amin to leucin, tyrosin, arginin, histidin, and the other amino-acids formed in pancreatic digestion of proteids. The physiological action of the several amins have been excellently worked out by Barger and Dale,¹² and their results explain many of the clinical symptoms observable in cases of intestinal toxemia, although their work was carried on with a view to obtaining the active principles of ergot, adrenalin chloride, etc.

Of the several amins, betaimidazolyethylamin, while it has a slight action on the blood pressure, has a specific action on unstripped muscle tissue, causing contraction of the uterus as well as a contraction of the bronchioles, resulting in great dyspnea and death in the rabbit and guinea-pig, from complete occlusion of air by the tonic spasm of the bronchioles. The isolation of this amin and its physiological action was accidentally discovered by Barger and Dale while investigating the action of ergot on the uterus. About the same time Kutscher¹³ discovered a base in extract of ergot which had the same action on the bronchioles. Ackermann,¹⁴ we find, was able to obtain the base by the putrefaction of histidin, while Windhaus and Voigt,¹⁵ in 1907, were able to obtain it synthetically from imidazolypropionic acid, according to the following steps:

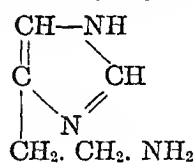
Imidazolypropionic acid.



Histidin.



Betaimidazolyethylamin.



Barger and Dale¹⁶ were later able to obtain this base from an extract of the intestinal mucosa of the ox, indicating that the base is absorbed by this means from the intestinal canal. The experiments carried on by Dale and Laidlaw¹⁷ to determine its physiological action were made with the base separated by them from ergot and from the intestinal mucosa, with the synthetic substance of Windhaus and Voigt¹⁸ and with the base of Ackermann and Kutscher,¹⁹ as well as with some of the base obtained by the putrefaction of histidin, the actions of which were all similar; so that their results can safely be accepted as representing the physiological action of betaimidazolyethylamin.

¹² Jour. Phys., 1910, xli, 1 and 2, 19.

¹⁴ Zeit. f. phys. Chem., 1910, Band lxxv, 504.

¹⁵ Bericht des Deut. Gesellschaft, 1907, xl, 3691.

¹⁶ Jour. Phys., 1910, xli, 494, No. 6.

¹⁸ Loc. cit.

¹³ Zentralbl. f. Physiol., 1910, xxiv, 163.

¹⁷ Ibid., 318, No. 5.

¹⁹ Zeit. f. Biol., 1910, Band liv, p. 387

Through the courtesy of Dr. Dale, I was able to obtain a large supply of the base for experimental purposes, and in this preliminary paper only a summary of the experimental work can be given, the details of which will appear in a later article, after a few further experiments have been completed. I obtained the identical results as Dale and Laidlaw,²⁰ namely, contraction of the uterus and bronchioles by intravenous injection, resulting in death from half a milligram in the guinea-pig, the animal dying in six minutes, with violent inspiratory efforts, the heart continuing to beat long after respiration had ceased. At post mortem the lungs were found pale and enormously distended and protruding from the thorax after section (Fig. 1). The spasm is so intense that when connected with a Meyer artificial respiration pump, no air can be forced in or drawn out of the lungs, the organ remaining permanently distended, as seen in anaphylaxis. In addition, I found that the same dose



FIG. 1.—Photograph of guinea-pig lungs after intravenous injection of 0.5 milligram of beta-imidazolylethylamin. Dark portions show normal lung tissue. Lighter portions are emphysematous.

administered into the trachea causes identical bronchial phenomena, while subcutaneous and intraperitoneal injections are much less toxic, suggesting that the action is entirely local on the unstriated muscle fiber and that the subcutaneous tissues have a detoxicating effect. Its action upon blood pressure and upon the uterus is not pertinent to the present subject, and I would refer anyone interested in this particular point to the paper by Dale and Laidlaw.²¹

Attempts so far to isolate the base from the blood of asthmatics have been unsuccessful, due to the many precipitations and filtrations; but experiments now in progress, I have reason to believe, will result in this being accomplished. However, I was able to

²⁰ Loc cit.

²¹ Loc cit.

isolate the base by Kutscher's method from three specimens of feces, but was unsuccessful in twelve other specimens, suggesting that the presence of the base in intestinal contents will vary according to diet and probably also with varying intestinal flora.

Injections of the urine of asthmatics, as well as the urine of normal guinea-pigs and rabbits, cause the characteristic bronchial spasm and death, with the characteristic postmortem appearance of the lungs above referred to (Fig. 2). The appearance of the lungs and the symptoms of the animal are similar to those dying from an anaphylactic shock, recalling the opinion of Meltzer²² that asthma is a condition of anaphylaxis. The delayed coagulation of the blood and the continuous fall of blood pressure observable in anaphylaxis is not found, however, after injections of betaimidazolylethylamin, although a lowered body temperature was uniformly observed.

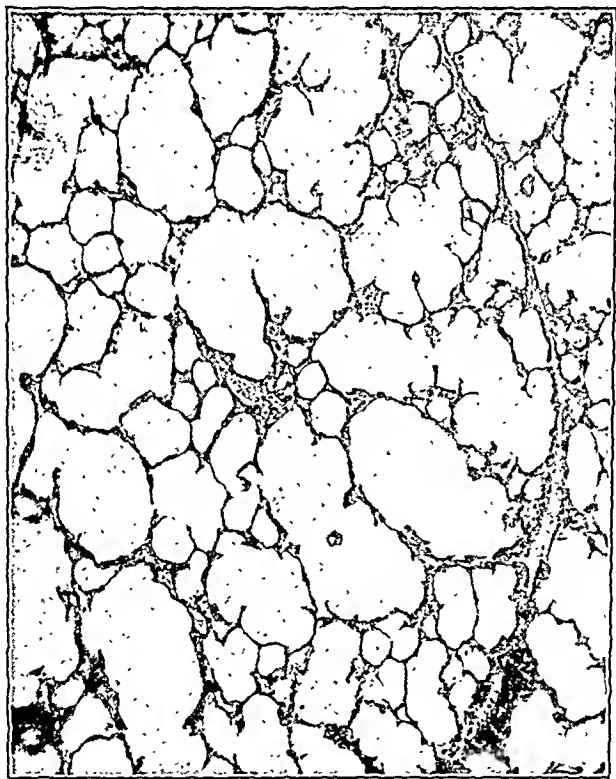


FIG. 2.—Photomicrograph of section of lung shown in Fig. 1. Note dilatation of air vesicles. 1 eye-piece and $\frac{2}{3}$ objective. $\times 87$.

However, no one has as yet fully explained the phenomena of anaphylactic shock, and it is possible that in injecting a foreign serum a mixture of nitrogenous toxic bases is also injected, which

²² Jour. Amer. Med. Assoc., 1910, IV, 1021-1024.

is ordinarily detoxicated, but which are not detoxicated by the tissues on the second injection of serum owing to the previous injection having exhausted this hypothetical detoxicating substance. From experiments, details of which will appear later, it appears that the normal human being, as well as the cat and dog, have the power of detoxicating not only betaimidazolylethylamin but also the other toxic amins formed by intestinal putrefaction, while the asthmatic individual has apparently lost this power.

We are accustomed to notice urticaria as evidence of intestinal toxemia, while the eosinophilia in asthma and anaphylaxis are frequent accompaniments of intestinal toxemia.

In my paper before the Louisiana State Medical Society in 1909, already referred to, I stated: "The fact that I have found evidence of auto-intoxication in every case of asthma examined by me for four years, leads me to believe that during the attack there is some toxin in the blood which acts similarly to the muscarin, or which depresses the respiratory centre to such an extent that the reflex stimulation of an inflamed nasal mucosa results in stimulation of the constrictor fibers of the vagus."

I now submit the above facts as bearing out, in part, my original contention, which I hope to be able to prove definitely in a short time by the isolation of this specific amin from the blood of asthmatics.

In closing, I wish to thank Dr. Maurice Couret, of the pathological department of Tulane University, for his kindness in taking the accompanying photographs.

**A RECURRENT DISEASE OF THE SKIN ASSOCIATED WITH
HIGH WINDS AND COLD WEATHER; FOR WHICH
THE NAME DERMATITIS HIEMALIS HAS
BEEN PROPOSED.**

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THE skin from its exposed condition is more influenced by extraneous conditions, such as climate, etc., than are other organs of the body. Many diseases of the skin are limited to certain

equatorial zones and others are greatly modified by climatic influences.

In 1874 Duhring¹ called attention to a pruritus, common in winter in certain regions of North America, which he called prurigo hiemalis. Hutchinson² and Hyde³ have also emphasized the influence of climate in certain dermatoses.

The condition herein described first attracted attention in 1883, since which time many cases have presented themselves for observation and study.

A report on the syndrome as observed in 14 cases was read before the International Medical Congress in Rome, in 1894, by one of the present writers, and later in the year it was presented before the American Dermatological Association. In 1896 a second report was read before the International Dermatological Congress in London. Again, in 1902, a more complete investigation of the condition was made, 9 additional cases being reported and carefully studied, both macroscopically and microscopically, especially in regard to the possible parasitic causation of the disease, as well as the relation it bears to an ordinary eczema.

These studies may be summarized as follows: Dermatitis hiemalis is a cutaneous eruption having definite clinical symptoms, following a fairly uniform course, and always associated with or limited to cold weather. It resembles eczema in that there is an inflammation, watery exudation, and some itching. Unlike eczema, however, it more frequently is accompanied by smarting, burning, and tingling. It disappears during the summer months and reappears the following autumn. The seat of predilection is the back of the hands, wrists, and more rarely the fingers; very rarely the feet, and never the trunk, arms, or thighs. Again, unlike eczema, the lesions are circumscribed, well defined, often with elevated edges, with a tendency to heal in the centre. All symptoms are aggravated by atmospheric changes, especially by storms and sudden variation of temperature. The lesions are very resistant to treatment, although they disappear spontaneously at the approach of summer or when the patient goes southward away from the lake region. Occupation or sex appear to have little to do with the condition. Careful examination for saprophytic organisms has invariably given negative results. From clinical studies the affection appears to be more closely allied to some of the erythemas than to eczema, and may be similar to if not identical with the condition referred to by Jonathan Hutchinson⁴ as "some peculiar eruptions allied to chilblains." Confirmatory is the suggestive bluish or purplish tint of the eruption that attacks the distal

¹ Philadelphia Med. Times, January 10, 1874.

² Clinical Lectures, London, 1879, i, 362.

³ Chicago Med. Jour. and Exam., 1885, 1, 187, and 1886, 3, 116.

⁴ Loc. cit.

extremities or parts farthest removed from the centres of circulation, and that it is met more frequently in the months in which there is the greatest variability in temperature. The histological findings are not distinctive, and the extent of the changes in the skin seems to be wholly dependent on the amount of the circulatory disturbances. This would lead one to infer that the disease is allied to eczema while characterized by some of the clinical features of chilblain. It presents, however, a distinct clinical picture which further observation may show is entitled to be looked on as a disease *sui generis*.

Since the presentation of the last paper many more cases have been observed, and we have made the following study, more especially on a few cases seen in the last two years. This work will be taken up under the following headings: (1) Etiology of the disease; (2) case histories; (3) a study of the histological findings, (4) the conditions of parakeratosis and acanthosis; (5) the course of pathological changes in the production of the disease; (6) treatment.

ETIOLOGY. At the International Medical Congress in Rome in 1894 it was questioned whether the etiological factor might not be found in one of the organisms of the tinea group, especially as the lesions were circumscribed and tended to heal in the centre. However, one of the writers, in conjunction with Dr. Henry S. Upson, presented a report on 4 cases before the International Dermatological Congress at London in 1896, in which it was shown that no pathogenic organisms were present. Moreover, such an etiological factor does not seem tenable, for if it were of parasitic origin it would undoubtedly affect other portions of the body and be carried from one person to another in the same family. This is not the case, for we have never seen 2 cases in the same family. Then, too, the affection is on an exposed part of the body which is very frequently cleansed, which again militates against the chance of such infection. Moreover, it occurs in winter, rather than in summer, a season unfavorable to the growth of organisms on exposed parts. During the past winter microscopic examinations of scrapings from several of the cases have been made, using ether to dissolve out the fat and a 10 per cent. potassium hydrate solution as clearing agent. In no case has any organism allied to the tinea group been found. Gram stains of the tissues in the latter stages of the disease have shown numerous gram positive skin cocci; but these, of course, are merely secondary invaders.

Having eliminated saprophytic organisms as a causative factor the influence of weather may be considered. Careful examination of the weather statistics for the last ten years shows that around the Great Lakes extreme daily variations in the thermometer are not any greater than in other parts of the country, for example, the inland cities of Cincinnati, Ohio, and Columbia, Missouri.

However, the weather is very variable, as may be easily shown. The average of the United States weather statistics for the last ten years shows that at Buffalo during the month of January, 14 per cent. of the days were rainy and 60 per cent. with snow, while 9 per cent. were foggy. There were also gales during 12 per cent. of the days and calms during 3 per cent. Cleveland during the same month had 13 per cent. of rainy days, 39 per cent. of snow, 4 per cent. of fogs, 9 per cent. of gales, and 6 per cent. of calms. During the month of March, averaged for ten years, Chicago had 24 per cent. of days with rain and a like percentage with snow, while 12 per cent. were foggy, 6 per cent. with gales, and 3 per cent. with calms. Buffalo during the same month had 22 per cent. of rainy days, 36 per cent. of snow, 15 per cent. of days with fog, 8 per cent. with gales, and 7 per cent. with calms. In Cleveland during the month of February the average for ten years shows the following: 13 per cent. of the days were rainy, 46 per cent. were accompanied with snowfall, 7 per cent. with fogs, 10 per cent. with gales, and 2 per cent. were calm days. These figures demonstrate the extreme variability of the winter weather about the Great Lakes.

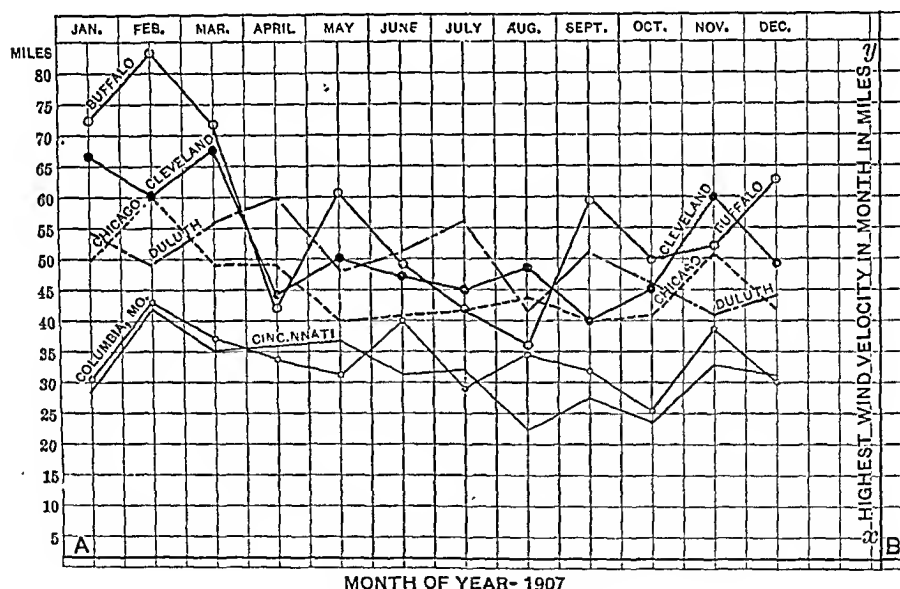


Fig. 1.—Highest velocity of wind in miles per hour.

In addition, this region is visited, especially during the winter months, with high winds. Examination of Fig. 1, taken from the report of the United States Weather Bureau for the year 1907, shows the highest velocity of the wind in miles per hour during the respective months, the lake cities, Buffalo, Chicago, Cleveland, and Duluth, being compared to the inland cities of Cincinnati, Ohio, and Columbia, Missouri.

It may be noted that the winds around the Great Lakes are especially high during the winter months and become somewhat lower during the months of June, July, August, and September. And not only are the winds of higher velocity in miles per hour, but examination of Fig. 2 will demonstrate that the total wind movement in miles per month is much greater in the cities of the Great Lake region than in the inland cities.

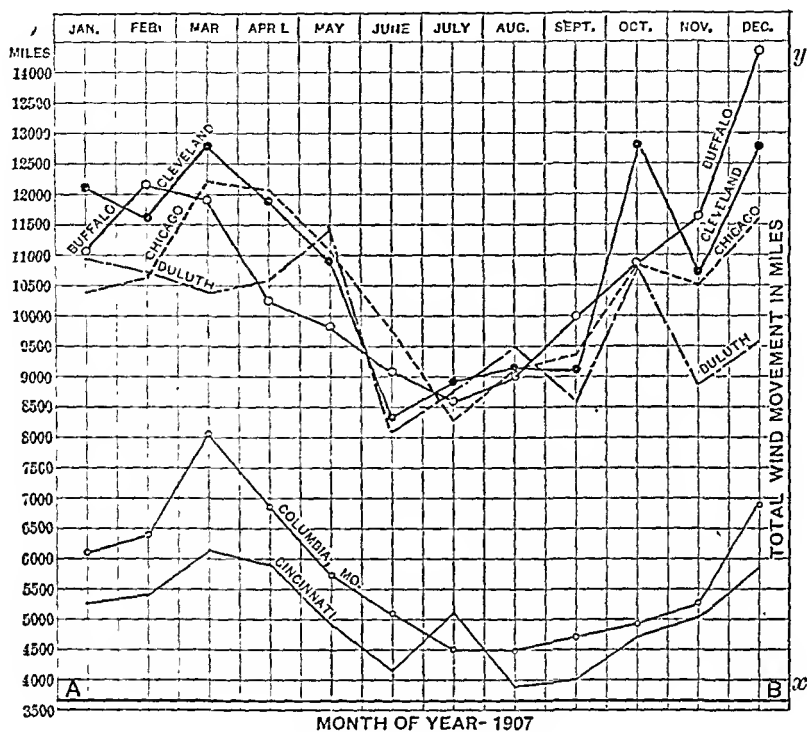


FIG. 2.—Total wind movement in miles per month.

To summarize, the winter climate around the Great Lakes, though not showing extreme changes in temperature in twenty-four hours, is very variable, especially in conjunction with the winds of high velocity and of high wind movement in miles per month.

CASE HISTORIES.

CASE I.—Female, aged twenty-three years; occupation housework. Aside from the present trouble the patient has always been well and strong. About two weeks before admission she first began to notice an itching, burning eruption which broke out on the back of one hand. Since then it has bothered her a great deal, and she has noticed a moist exudate at times. At the time of writing there is an area about 2×2 cm. on the back of the left hand, and a smaller one on the right wrist. Both areas are circinate, well defined, with

slightly elevated edges, and a tendency to heal in their centres. As yet there is verly little crust formation, but one sees some cracking of the surfaces and a little serous exudate. The areas are of a dark red color and show no induration. Patient says none in the family are troubled with a like affection, and she has never had it before.

CASE II.—George S., aged twenty-one years; switchman. The family and personal histories are negative. Patient had an infection of the second finger of the right hand three years ago, and ever since there has been a scaling and cracking of the skin over this area. About three months before admission an eruption broke out at the base of the third finger of the left hand and the like finger of the right. The lesions have extended a little, and a month later another lesion appeared on his right forearm. Patient was admitted to Lakeside Hospital for study. The blood showed at that time 3 per cent. of eosinophiles, otherwise nothing out of the ordinary was found. The lesions were similar to those of Case I except that there was crust formation and more induration of the areas. A biopsy was made of several fresh papules found on the affected area of the forearm. The finger involved for three years showed merely a chronic eczema, illustrating the fact that an eczema and a dermatitis hiemalis may be present on the same patient.

CASE III.—Carl W., aged thirty years; baker. Patient is a Bohemian, and was never troubled with this disease until last year, when he came to this country and settled in Detroit. The disease was present all winter, disappearing the summer following, only to appear again the next October. Patient came to Cleveland, hoping to be relieved of the trouble, but he has been troubled off and on for the last five months. The eruption itches and burns a great deal, and there is more or less of a moist exudation. The areas bleed quite easily; otherwise he feels perfectly well. Both posterior surfaces of the hands and one wrist are affected with well-defined, circinate, dark red lesions, showing an elevated edge and a noticeable tendency to heal in their centres. Crust formation is quite marked, and there is some induration of the parts. A biopsy was made of an area about three or four weeks old, and also from a spot of more recent appearance.

CASE IV.—G. W. P., aged thirty-five years; bookkeeper. His habits are good, and he has always been well, except for the present trouble. For the last ten years the patient has been bothered every year with an itching, burning eruption, which is limited to the hands, and is present only during the winter. It appears early or late in the fall, according to the severity of the weather, as he has himself noticed, and lasts until spring. At times the lesions will partially heal, but only to reappear, and he has never found anything that gave him much relief. He says he has never changed climate during the winter, so does not know what effect another climate would have on the condition. No others of the family are

troubled. The lesions on the back of the hands are quite extensive, but always well defined, and with a marked tendency to heal in the centre. The skin is quite thick, and there appears to be an hypertrophy of the upper layers. A biopsy was made of two areas of several months' duration.

It might be said that all the patients mentioned returned at more or less regular intervals during the winter. Their lesions would partially heal up at times, only to reappear, despite treatment. However, with the return of spring all of them immediately began to improve, and with the exception of Case III, all were well by the last of May. Case III reported himself well the middle of June.

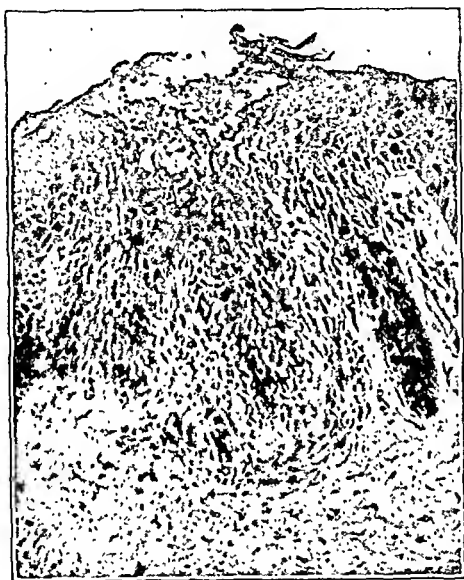


FIG. 3.—Early lesion. $\times 140$. Bursting of a superficial vesicle, with marked edema and infiltration of the papillæ and epidermis with leukocytes.

A STUDY OF THE HISTOLOGICAL FINDINGS. A. *Early Lesion*. The lesion was taken from Case I. In the area of the section showing the least change from the normal (Fig. 3) we find the stratum corneum about 4 to 5 cells thick, in which the individual cells are made out with difficulty and most of the nuclei not at all. There is a stratum lucidum 1 or 2 cells thick in which the nuclei are absent and the cells are filled with fine granules. The stratum granulosum is 4 to 6 cells in depth and the cells show shrunken, hyperchromatic nuclei and masses of extruded chromatin in their protoplasm. The stratum spinosum under this is about 13 cells in thickness over the papillæ and 24 in the interpapillary processes of the epidermis. These cells are normal in appearance. The papillæ under this area show merely enlarged vessels with swollen endothelial cells and a slight perivascular edema. There is no perivascular cellular exudate.

A short distance from the area already described we come to a field where further changes have taken place (Fig. 8). Here the stratum corneum (*a*), about 5 cells thick, is made up of compressed, coherent cells; still containing their shrunken hyperchromatic

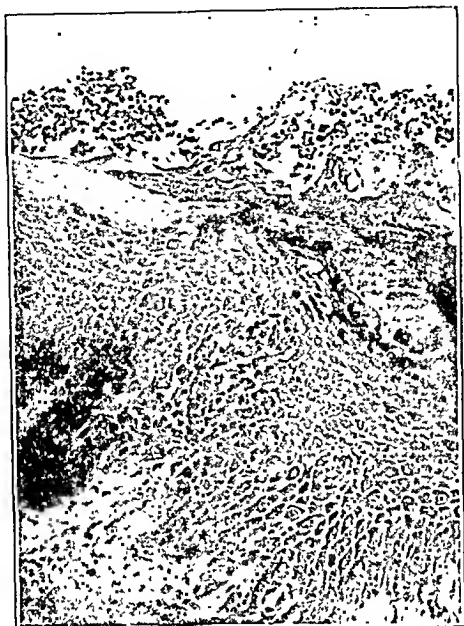


FIG. 4.—Moderately early lesion. $\times 120$. Vesicle deep in the epidermis, with superficial crust formation. Stratum spinosum swollen and hypertrophied.



FIG. 5.—Height of process. $\times 70$. Superficial crust formation and papillary vessel greatly dilated. Epidermis shows edema, acanthosis, and infiltration, with leukocytes.

nuclei. Intercellular spaces are seen between the lamellæ, probably filled with more or less fluid. The stratum lucidum (*b*) is scarcely discernible, and the stratum granulosum (*c*), 2 to 3 or 4 cells thick at one end of the figure, has nearly disappeared at the other end.

Still further changes are shown in Fig. 9, where neither the stratum granulosum nor lucidum are to be made out, and numerous small vaeuolated areas are found under the lamellæ of the corneum. The latter, here 4 or 5 cells in thickness, still retains its nuelei and appears moderately lamellated. The priekle cell layer under this is from 13 cells in thickness over the papillæ to 28 cells in the inter-papillary epidermis. The cells of the stratum spinosum over the papillæ are very much separated by edema, and about the middle of the stratum there is an area where the strain on the intercellular bridges has finally become so marked that they have broken, resulting in a vesicle formation, containing a few polymorpho-nuclear leukocytes, shrunken cells, and nuelei (Fig. 10). Deeper in



FIG. 6.—Chronic process. $\times 70$. Intense parakeratosis and acanthosis. Marked leukocytic infiltration around the vessels of the corium.

the epidermis, between the papillæ, the edema is not so marked, and the cells are merely more or less separated. The edema is mostly extracellular in type. The papillæ in the region are very edematous, the vessels are enlarged, and their endothelial cells swollen, while there is an exudate of cells and fluid which have extended, not only into the papillary tissue, but also outward between the cells of the nearby stratum spinosum. The cellular exudate is mostly polymorphonuclear, with a few small mononuclears; indicating an acute process. The deep corium reveals little outside of a like condition around the vessels. There is no change in the collagen or elastic fibers.

B. *More Advanced Lesion.* This section was removed from an old lesion on the arm of Case II, as a few new papules had formed on it. Only the fresh lesion will be described.

At about the centre of the section (Fig. 4) there is quite a perceptible elevation of the epidermis. One notices at once the heavy edema and cellular exudate in the immediate vicinity. The stratum corneum consists of only 2 or 3 strands of flattened, nucleated cells which have been forced apart, as it were, by some pressure from below. Beneath them there is an open area dipping down into the epidermis, which contains mostly red blood cells, coagulated fibrin, and a few fragments of broken down epidermic cells. From this ruptured vesicle definite intercellular spaces lead down to the edematous papilla, although the spaces are clogged with an exudate

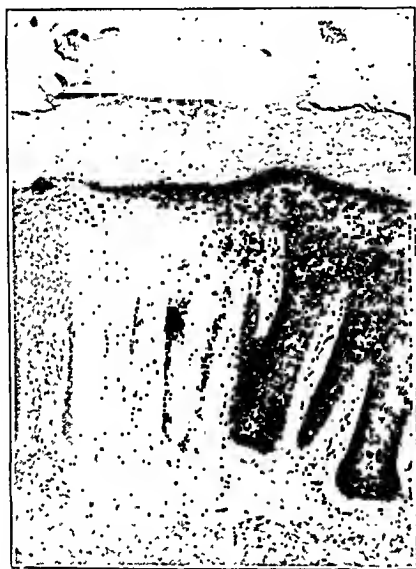


FIG. 7.—Healing process. $\times 70$. Old crust on new-formed normal stratum corneum. Acanthosis of epidermis. Infiltration and thickening of vessels of corium.

of leukocytes and red blood cells. There is no stratum granulosum or lucidum and the stratum spinosum is about 8 cells thick over the papillæ and 16 to 18 cells thick over the interpapillary spaces. There is a marked general extracellular edema of the stratum spinosum, very few mitoses are seen, and the deeply staining nuclei are somewhat shrunken from their cell boundaries.

Corium: The papillæ in the area involved show enlarged vessels, with swollen endothelial cells. There is a marked edema of the perivascular tissue and a cellular exudation, mostly of polymorphonuclear leukocytes and red blood cells. The collagen fibers are swollen and stain poorly, while the nuclei are few and compressed. Elastic fibers are very fine. The vessels in the deeper corium will not be described at this time as they show the same results as observed in the older processes.

C. Intermediate Stage. In a stage slightly more advanced than the last, found in a section of tissue from a patient suffering from this particular lesion for two weeks, the following is noted: At one end of the section there is a large crust replacing the stratum corneum, and even thicker than the epidermis, being made up of coagulated fibrin, broken-down cells and nuclei, red blood cells, and numerous large gram positive skin cocci. Here and there one or two cells with shrunken nuclei and a partial extrusion of chromatin show us what should be the stratum granulosum. The stratum lucidum is absent. The stratum spinosum is about 12 cells thick over the papillæ and about 18 cells in thickness in the interpapillary epidermis. It gives one the impression of being swollen, which is accounted for by the marked intercellular edema,

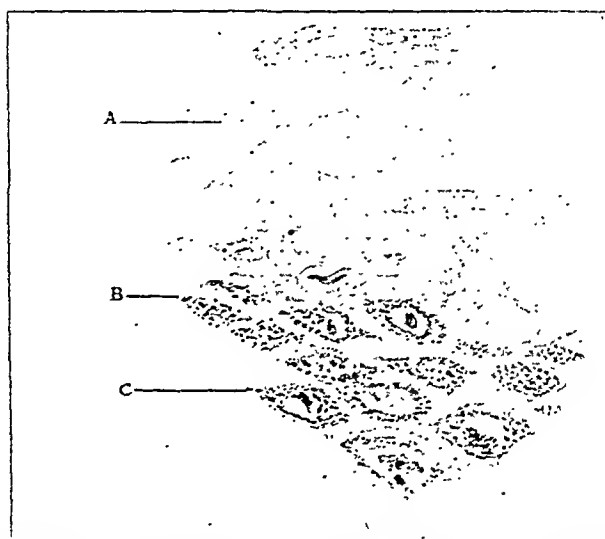


FIG. 8.—Earliest lesion, showing normal process of cornification. Superficial area of middle of the epidermis of same section as in Fig. 3. A, stratum corneum; B, stratum lucidum; C, stratum granulosum. All drawings—Figs. 8 to 12—were made with a Spencer camera lucida, Leitz 4 ocular and Leitz 12 objective, giving a uniform magnification of 1575 diameters.

while at one area there is a deep vesicle formation, in which coagulated fibrin, broken down cells, nuclei, and red blood cells are seen. Some of the red cells are noticed to have travelled out between the intercellular spaces of the stratum spinosum, the cells of which appear to be larger and better nourished than normally. Numerous mitotic figures are seen and several amitotic divisions are observed (Fig. 11), a very unusual condition, indicating the rapid multiplication of the cells. The vessels supplying this portion of the section are dilated, giving indication of a large vascular supply to the part. In addition to the changes already described in the previous sections a larger proportion of small mononuclear cells are present in the perivascular exudate, indicating a beginning chronic process of inflammation. At this stage the collagen fibers are beginning to

stain poorly, and they are forced apart by the edema of the tissues. No nerve tissue is observed.

D. *Height of the Process.* This is shown in a section of tissue from the same patient, but it exhibits a more marked change. It was removed from the posterior surface of the left hand.

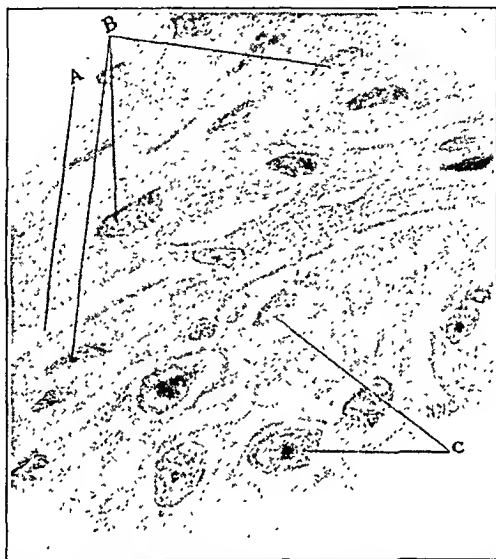


FIG. 9.—Earliest lesion, to show absence of stratum granulosum stratum ludium. *A*, inter-lamellar vesicle formation; *B*, slightly hyperchromatic, persistent nuclei of lamellated stratum corneum; *C*, persistent stratum spinosum.

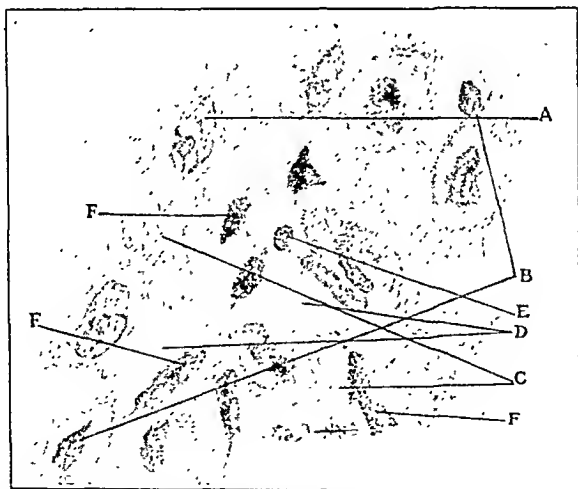


FIG. 10.—Early lesion. Superficial vesicle of prickle-cell layer below Fig. 4. *A*, normal prickle cell; *B*, shrunken nuclei of cells with intracellular edema; *C*, extracellular edema; *D*, vesicle formation; *E*, lymphocyte; *F*, shrunken nuclei.

On examination with the low power one is immediately struck by the heavy vascular supply of the parts (Fig. 5). A large crust extending nearly the entire distance across the section is made up of the same elements as the crust already described. There is no

stratum granulosum or stratum lucidum, but rather vacuolated areas filled with fibrin and more or less cellular exudate. Definite intercellular spaces lead down through the edematous prickle-cell layer to the very edematous, injected papillæ. These spaces are clogged with red blood cells and polymorphonuclear and small mononuclear leukocytes. The stratum spinosum is 6 to 8 cells thick over the papillæ and from 35 to 40 cells in thickness in the interpapillary epidermis. It is made up of large swollen cells showing numerous mitoses, the cells being separated more or less by edema. However, the edematous condition is more marked above the papillæ. These have an intense vascular supply and a perivascular edema that has entirely separated the tissues. The latter shows a very large cellular infiltration. The vessels in the deeper corium show a like condition, and there is a slight thickening of their walls; now and then a young fibroblast being seen. The collagen and elastic fibers show no changes not already described. No nerve tissue is seen.

E. *First Stage of the End Process.* This section to be described was removed from a chronic hypertrophied area from the hand of Case IV.

Examination even with a low-power lens shows a marked thickening of the stratum corneum and a great depth to the interpapillary epidermal processes. Near the centre of the section the following condition is observed: There is a stratum corneum (Fig. 6) about 40 to 45 cells in thickness, made up of flattened, incompletely dried-out cells in which the shrunken, hyperchromatic nuclei are still present. The stratum spinosum is about 35 to 40 cells thick between the papillæ and 10 to 12 cells thick over them. A layer of 2 or 3 cells showing a defective extrusion of chromatin from their shrunken nuclei gives evidence of a beginning formation of the stratum granulosum. There is no edema of the epidermis and no infiltration with cells. A few mitoses are seen, indicating a slightly increased nutrition of the part. The corium shows nearly the same condition as in the former section, and the type of cellular exudate around a papillary vessel is shown in Fig. 12. But at this stage the vascular supply is not so extensive and the vessel walls show some thickening, occasionally a young fibroblast being seen.

F. *Final Stage of the End Process.* This section is from an area on the hand of Case IV, and is of several months' duration (Fig. 7).

There is a stratum corneum about 12 cells thick, in which the outlines of the cells can still be made out, though with difficulty, and the nuclei exist only as empty spaces, having lost all their chromatin. Near the centre of the section there is a large dense crust, as thick as the horny layer, and superimposed upon it. There is a nearly normal stratum granulosum 3 or 4 cells thick and a stratum lucidum 1 or 2 cells in thickness. The prickle-cell

layers shows a definite acanthosis from the long-increased blood supply, and is about 15 cells in thickness over the papillæ, and from 30 to 32 cells thick between them. There is very little inter-cellular edema and none intracellular. The cells are large, and appear to be well supplied with nourishment, and one amitotic

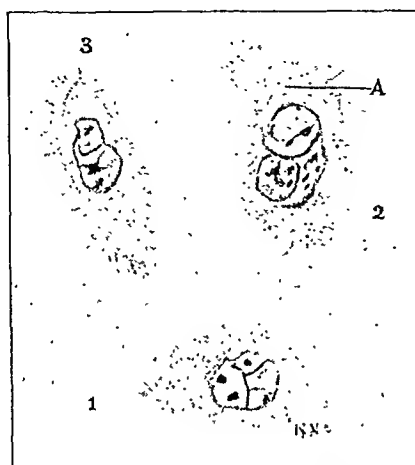


FIG. 11.—Moderately early condition, from portion of same area as Fig. 4, and showing cell division by amitosis. A, beginning vacuolar degeneration.

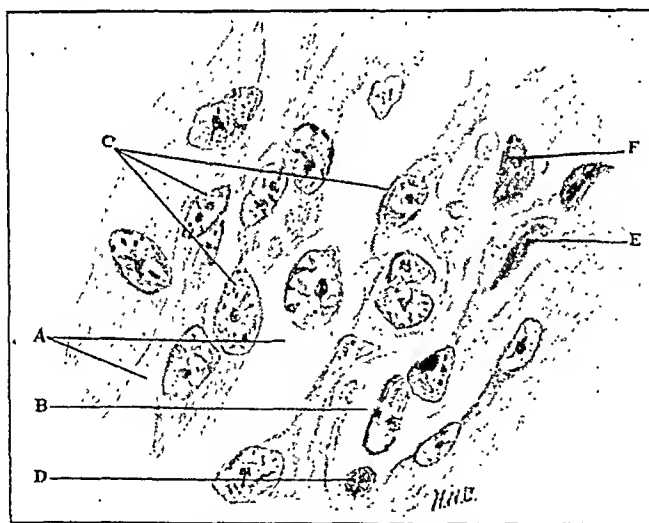


FIG. 12.—Chronic process. Portion of middle of papilla from same area as Fig. 6. A, dilated vessels; B, perivascular edema; C, swollen endothelial cells; D, lymphocyte; E, shrunken nucleus; F, large mononuclear cell.

division is observed. The vessels of the papillæ are still moderately dilated and have swollen endothelial cells. Still there is very little exudation of serum and only a few perivascular elements, mostly small mononuclears and young fibroblasts. The collagen fibers of the corium are still swollen and forced apart, but they are beginning to stain more readily. The elastic fibers are fine and not

forced apart so much as in previous sections. No nerve elements are seen. The vessels of the corium show thickened walls and swollen endothelial cells lining them, while a few young fibroblasts are seen in the walls. Their intense perivascular exudate is mostly small mononuclear cells and a few young fibroblasts; now and then an eosinophile is seen.

PRODUCTION OF THE CONDITIONS OF PARAKERATOSIS AND ACANTHOSIS. Before taking up the study of the course of events in the different stages of this condition it may be well to review the subjects of parakeratosis and acanthosis somewhat in detail, especially as they have an important bearing on the findings of this condition in its different stages. As already emphasized by Corlett and Schultz,⁵ "cornification is not a process of specialization and differentiation but of gradually progressing physiological degeneration, which leads ultimately to death." Apparently the only functions preserved by the epidermal cells are nutrition and multiplication, and as they get further from their papillary blood supply they lose first their power of multiplication and later that of nutrition. The cells then begin to dry up and their nuclei shrink and become hyperchromatic. This nuclear chromatic material is then partially extruded from the nucleus, from disturbance of the cell-nucleus balance, resulting in the coarsely granular cells of the stratum granulosum. Later it is entirely extruded and finely distributed through the protoplasm, while the nucleus disappears entirely, cells of the stratum lucidum type. In the final death of the cell the chromatin disappears entirely and the cells of the stratum corneum are mere dried up, horny lamellæ.

However, if there is an edema of the tissues with resulting increased nutrition of the epidermal cells, we will find a disturbance in the process of cornification. The cells not only are able to multiply for a longer period than normally, but they retain the power to assimilate nutrition and fluid. Consequently, they do not become dried up until they reach the surface, so that no cells of the stratum granulosum or stratum lucidum type are formed. At the surface the rapid, only partial drying-out process results in the formation of nucleated, horny lamellæ. All variations between this condition of parakeratosis and the normal may be found, depending on the degree of edema of the parts.

The phenomena of acanthosis are likewise dependent in part on the increased nutrition of the cells. As Unna⁶ has already pointed out, in the normal epidermis from one-fourth to one-third of the epidermal mitoses takes place in a middle zone of the stratum spinosum and from two-thirds to three-fourths in the two lower layers of cells of the epidermis. But in a condition of edema where

⁵ Jour. Cutan. Dis., February, 1909.

⁶ Die Histopathologie der Hautkrankheiten, Berlin, 1894, s. 201.

all the cells are bathed in an increased nutritious serum, they retain their multiplicative and assimilative capacities longer than usual, and we find many mitoses, even but a few cells deep from the external surface. Consequently, more cells are formed, they are larger, and live longer than normally. Hence the epidermis is thickened, and is found not only to extend further upward, but the inter-papillary processes even extend deeper into the corium, and we have acanthosis.

THE CHANGES OBSERVED IN THE PRODUCTION OF THE LESIONS. We are now ready to explain the course of events in the production of the lesions. Given a susceptible person the variable, wintry, windy weather, as met with in the Great Lake region of North America causes an irritation of the skin of the hands, resulting first in a slight vascular dilatation of the vessels of the papillæ. The endothelial cells lining the vessels swell up, and if the condition continues there will result the extravasation of some serum from these vessels into the papillary tissue. Possibly a few polymorphonuclear leukocytes will also find their way into the surrounding tissues. The irritation still continuing, there will be a constantly increasing vascular dilatation, and a larger amount of serum being poured out, it will gradually work out through the lymph channels of the epidermis, resulting in a higher or lower grade of edema. And, as has been shown, even a slight grade of edema will exercise quite a marked influence on the process of cornification, resulting in a parakeratosis. The process of exudation of the serum from the papillary capillaries, with the passage out of leukocytes and red blood cells, may be very rapid in its course. Then this exudate, working out from the papillæ, through the lymph channels into the epidermis, may cause such a sudden strain on the intercellular bridges of the prickle cells that they are no longer able to withstand, and they burst. Such a condition we find in Fig. 10, when the vesicle is deep in the stratum spinosum. However, suppose the edematous area is situated high up in the epidermis and that the area is covered only by a few layers of rapidly and incompletely cornified cells. Then when the pressure becomes too great the vesicle may break outward and we find such a picture as is shown in Fig. 3, the vesicle containing fibrin, broken-down leukocytes, and red blood cells. Such an exposed area is soon changed into a crust of coagulated serum, broken-down epithelium, nuclei, red cells, and leukocytes. This is the height of the process, and at this time we almost invariably find a secondary growth of Gram-positive skin cocci in the crust. There are also more or less changes in the deep corium, due to the etiological factor before mentioned, in connection with the irritation of broken-down cellular products, etc. Here, too, the vessels become dilated, the endothelial cells swollen, and an exudate of serum and polymorphonuclear cells is poured out into the surrounding tissues, resulting

in a perivascular edema and inflammation. Indeed, the perivascular edema may be so marked at this time that the tissues are entirely forced apart and broken up.

Again, suppose the irritation has continued for some time, then we will find an even more severe type of change around the vessels of the corium. There is a heavy exudate of serum and leukocytes, the latter mostly small in type, with an occasional eosinophile and endothelial cell. The collagen fibers are swollen, forced apart, and stain poorly, while their nuclei are flattened from the pressure of serum in the tissues. The elastic fibers are also forced apart. The result of the copious supply of serum from the papillary vessels to the epidermis is that the cells receive better nutrition than normal, so that they are continually bathed in serum. Instead of drying up they will continue to assimilate nutrition and to multiply, both by direct and indirect division. The result is the production of a thickened epidermis, showing an atypical process of cornification, parakeratosis. Moreover, examination shows us long interpapillary processes of epidermis made up of large, healthy looking cells, showing numerous mitoses and apparently growing down into the corium as well as upward, acanthosis. This is the intermediate step between the acute and the chronic process as shown in Fig. 6, Crusts may or may not be present.

As the chronic stage begins to appear we find certain vascular changes that have a very important bearing. From the long-continued irritation we not only have the perivascular exudate already spoken of, but, as in Fig. 12, the vessel walls become thickened and a few young fibroblasts are seen in the walls and in the surrounding tissues. This thickening of the vessel walls tends to reduce the blood supply and consequently the edema, so that once more we have a return of the tissues to the normal, from the decreased vascular supply. Such a condition is shown in Fig. 7, where a thickened, evidently long-irritated epidermis is shown undergoing a normal process of cornification, though it still retains a crust above it, revealing an old process as yet incomplete.

Either the healing takes place through a process of chronic inflammation, as outlined above, or at the approach of spring the changeable, windy weather no longer irritates the susceptible parts, so that even though the process be acute, by removing the causative factor the condition tends to subside from lessened blood supply, and thus a return to the normal is found.

TREATMENT. Of this little need be said, as no treatment seems to have much effect, at least not for any length of time. The general hygienic care of the skin should be enjoined, together with such protective measures as the wearing of leather gloves, etc. No special internal medication has been found of any avail. Locally, diachylon ointment with salicylic acid, varying in strength from 3 to 10 grains to the ounce, may be used, often with good results for

the time being. At times, Lassar's paste seems to work well, while the boric acid ointment (U. S. P.) or the white precipitate ointment, 5 per cent., may be used. As a prophylactic to those predisposed simple protective applications of petrolatum and paraffine are indicated on the approach of cold weather. In all cases the patient should be cautioned to keep the hands out of water as much as possible, and to avoid all local irritants. The ideal treatment to be advised is a change of climate to a warmer region, a treatment always followed with a disappearance of the trouble.

In conclusion we wish to thank Dr. O. T. Schultz, of the Pathological Department of the Western Reserve University, for his valuable assistance and suggestions in the histological study of this paper. To him also thanks are due for the taking of the photomicrographs.

EXPERIMENTAL STUDY OF THE EFFECTS OF URETERAL OBSTRUCTION ON KIDNEY FUNCTION AND STRUCTURE.¹

BY EDWIN BEER, M.D.,

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THE following work was begun over four years ago, to determine, if possible, how long a ureter might be tied off, before making an ureterovesical anastomosis, without sacrificing the involved kidney's functional integrity. In the course of difficult pelvic dissections it is well known that the ureters are occasionally injured and at times the attempt to repair the damage protracts the original operation to a dangerous degree. To avoid this prolongation, numerous operators have resorted to direct ligation of the involved ureter² above the point of injury, relying upon the natural process of atrophy to take care of the thus excluded kidney. If an operator is thus forced to exclude the kidney of one side, either actuated by such doubts as are engendered by undue prolongation of the operation, or by reason of the fact that the operative technique appears to be too difficult, the possibility of a later operation anastomosing the excluded side with the bladder has been completely ignored, so far as I have been able to discover in a study of the literature. To determine how long such a kidney could wait without losing its functional adequacy was the original impulse for this study, in the course of which many other interesting points developed. In this paper I expect, therefore, as briefly as possible,

¹ Read before the Surgical Section of the New York Academy of Medicine, 1912.

² L. Landau, *Deut. med. Woch.*, 1900; Wassiljew, *Deut. Zeit. f. Chirurgie*, 1907, lxxxix; A. V. Rosthorn, *Jour. Amer. Med. Assoc.*, 1906, p. 1881.

to bring all these facts together without extensive narration of numerous experimental details involved.

All the work was done on some 60 dogs in the surgical research laboratory of Columbia University. To the gentlemen in charge of this laboratory, as well as the students who assisted me, I owe a debt of gratitude, which I gladly take this opportunity to express.

I. HYDRONEPHROSIS MAY RESULT FROM INFECTION OF THE URETEROPELVIC TRACT WITHOUT STENOSIS. A series of experiments was made with the object of determining the effect of direct injection of cultures into the ureter after extraperitoneal exposure of the same without in any way injuring its lumen by artificial stenosis. Colon bacilli were injected through a fine needle. The involved kidney and ureter were removed at varying times, and regularly showed well-marked hydronephrosis and hydroureter. In the earliest case the kidney was examined nine days after the injection, and the organ was enlarged and the pelvis moderately dilated. In another case, after fourteen days, the kidney was removed and it was practically normal, except for well-marked hydronephrosis. In another case, after twenty-one days, a good-sized hydronephrotic sac was present.

In none of the cases were abscesses produced in the kidney parenchyma.

II. HYDROURETER AND HYDRONEPHROSIS OF AN EXTREME DEGREE, IN TIME LEADING TO COMPLETE PARENCHYMATOUS ATROPHY, FOLLOW INJECTION OF INFECTIOUS ORGANISMS ABOVE A STENOSIS. If the same technique is followed as was used in Group I plus complete or incomplete ligation of the ureter, whether with *catgut* or with *silk*, an extreme degree of distention of the pelvis and ureter follow, unless the injected bacteria are too virulent, when pyonephrosis or pyelonephritis and early death follow. The early pictures are very much as in group I. Thus already in five days a moderate hydronephrosis has developed. In another case in eleven days there was a marked dilatation with some perinephritis. In another in twelve days, the same picture. In cases lasting thirty-five days a very large hydronephrotic sac developed despite the use of a catgut ligature in producing the stenosis. In still another case, after fifty-six days, nothing but a large sac was left representing the destroyed organ.

III. AFTER DEVELOPING A PRIMARY HYDROURETER AND HYDRONEPHROSIS OF A MILD DEGREE, THE KIDNEY UNDERGOES ATROPHY IF THE URETER IS TIED AND NO INFECTION IS SUPERADDED. If the same technique is used as in group II, and no organisms are introduced into the ureter, there is a primary dilatation above the stenosis, which gradually recedes after the first two or three weeks, and then the pelvis becomes folded on itself and the kidney parenchyma gradually atrophies. This atrophy becomes so complete that at the end of five months (Case 9) the excluded kidney is

nothing more than a firm fibrous mass, measuring from pole to pole one inch and from sinus to convexity one-half inch, with folded enlarged pelvis and ureter. These phenomena are of importance in connection with the problem which led to this series of experiments, as they bear upon the essential question that is involved, that is, the functional adequacy of an excluded kidney.

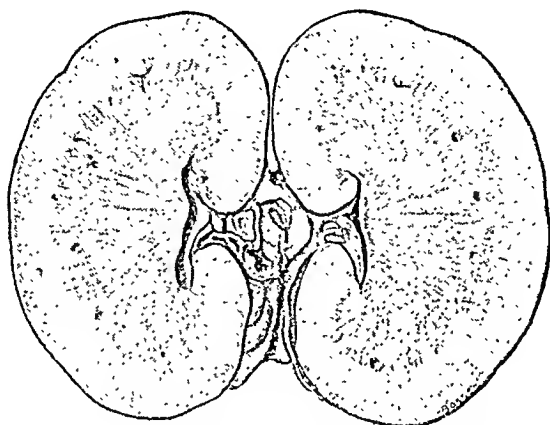


FIG. 1.—Normal kidney with slit-like pelvis.

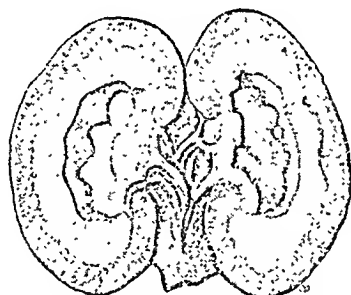


FIG. 2.—Atrophic kidney, three months after ligation; no infection.

From this series of observations it seemed likely that the excluded organ was able to secrete up to about the third week as evidenced by the dilatation and distention of pelvis and ureter up to this date. It also appeared that after these three weeks the function was materially impaired as the distention, probably an evidence of secretory activity, disappeared. Chemical examination of the fluid in the distended ureter showed varying amounts of urea, which seemed corroborative of this view point. Fluid removed three weeks after ligation showed no urea in one case; in another, twenty-four days after ligation, only 0.005 gram per cubic centimeter, whereas fourteen days after exclusion in another case the urea was as high as 5 per cent.

IV. IF A KIDNEY IS EXCLUDED UP TO THREE TO FOUR WEEKS AND THEN ITS URETER IS REIMPLANTED IN THE BLADDER, THE KIDNEY SEEMS CAPABLE OF CARRYING ON ALL THE EXCRETORY

WORK OF BOTH ORGANS. To adequately test the functional capacity of the reimplanted kidney, it was necessary to remove the other kidney. Cystoscopic examinations with indigo carmine, though repeatedly made, I did not accept as conclusive evidence

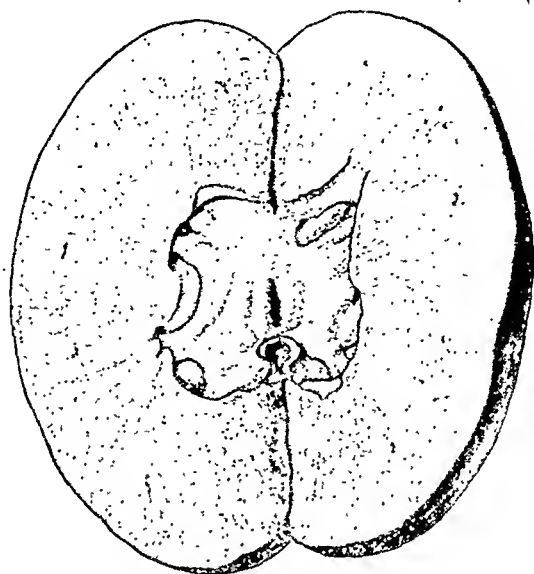


FIG. 3.—Two weeks after ligation plus infection (hydronephrosis).

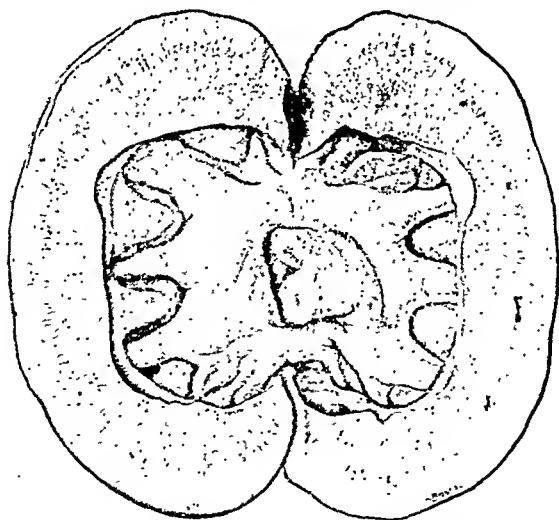


FIG. 4.—Four weeks after ligation of ureter plus infection (hydronephrosis).

of renal adequacy or inadequacy. Consequently the most exacting test was resorted to and nephrectomy of the second organ performed. In human surgery we will not be called upon to perform any such test, nor is such a degree of adequacy required. If one can reimplant an excluded kidney that has only 50 per cent. of

the total renal capacity it is that much gain, as all cases coming into this category must have a second adequate organ.

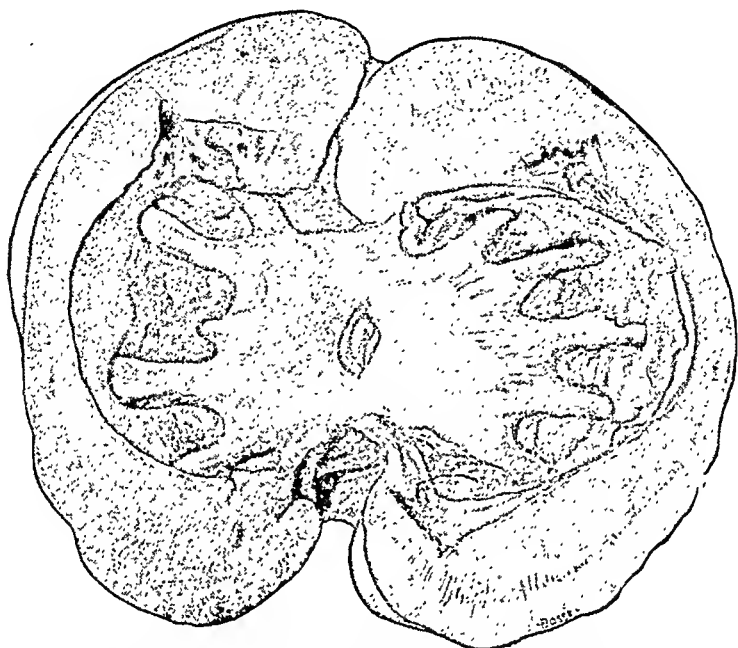


FIG. 5.—No. 226. Exclusion of three weeks. After nephrectomy of the other organ animal lived on this kidney until the ureter became plugged with a calculus, almost two months after removal of second kidney.

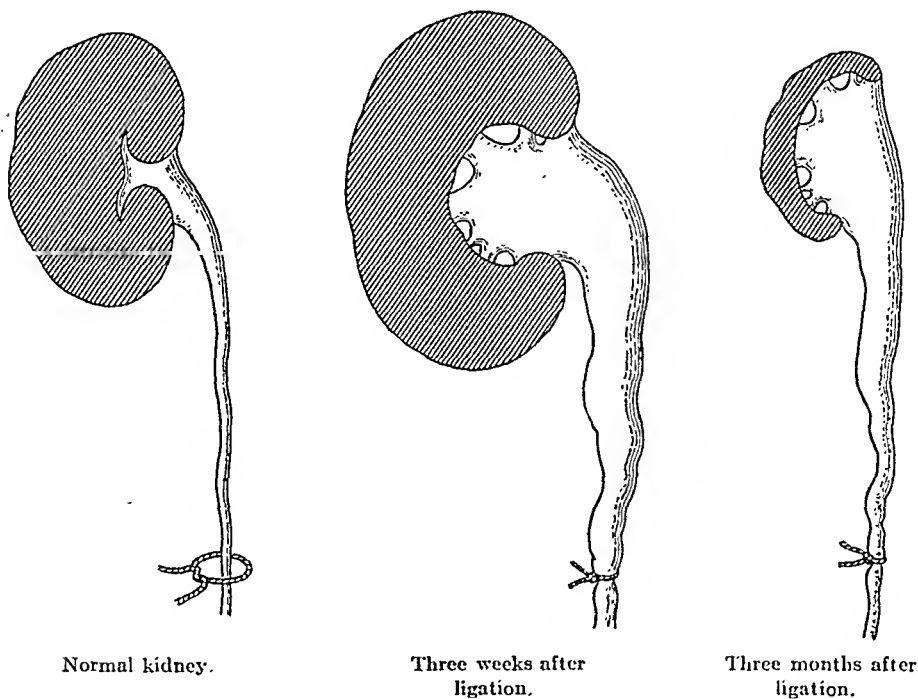


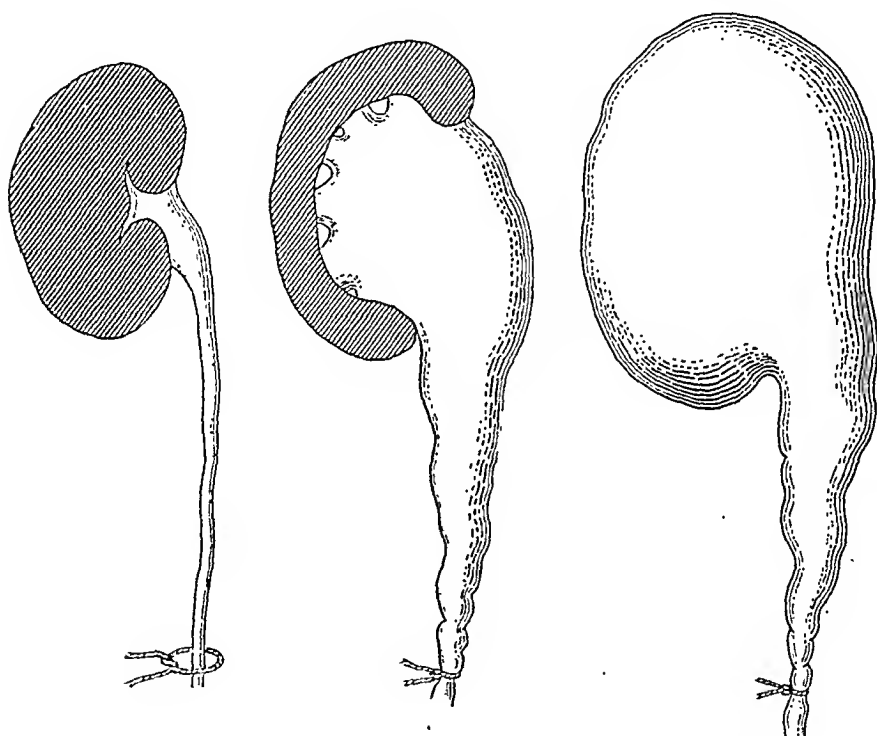
FIG. 6.—Aseptic series.

To demonstrate the evidence upon which the conclusions just mentioned are based, I shall report several experiments in detail. The accompanying drawings, Figs. 1 to 7, from specimens, together with the diagrams, illustrate well the processes just described.

Experiment. (215) Male dog.

March 24, 1909. First operation. Through low laparotomy the right ureter was exposed at insertion into bladder. Silk ligature tied at this point.

March 31, 1909. A low left-sided Kammerer incision. Bladder drawn into wound after separating omental adhesions. The



Normal kidney.

Three weeks after
ligation.

Three months after
ligation.

FIG. 7.—Septic series.

ureter was found dilated moderately with clear amber-colored fluid. An anastomosis of ureter and bladder was made, side to side, by means of a silk ligature (McGraw technique), reinforced with Lembert sutures.

April 24, 1909. Dog in fine condition

May 29, 1909. Left lumbar nephrectomy.

September 1, 1909. Dog died.

Autopsy. Bladder contains amber-colored fluid; specific gravity 1024; urea 0.2 per cent.; alkaline; microscopically, many pus cells and inorganic salts. The pelvis of the kidney and ureter contain mucopus full of gravel. The parenchyma shows numerous abscesses.

The pelvis is dilated. The new opening in the bladder is surrounded by edematous tissue, which has stenosed it, preventing ready emptying of distended ureter into bladder.

Remarks. In this dog the right kidney was excluded for one week and then the corresponding ureter was implanted in the bladder. After the dog had thoroughly recovered from these operations the adequacy of this kidney was tested by removing the left kidney. The dog continued to live for over three months, showing no signs of renal insufficiency. Had not infection supervened death might not have resulted when it did. In brief, this dog's right kidney, though it had been excluded from work for seven days, was capable of carrying on all the renal excretory work of the organism.

Experiment. (226). Male dog.

April 3, 1909. First operation. Right ureter exposed close to bladder by transperitoneal route, and ligated.

April 17, 1909. In excellent condition.

April 24, 1909. Three weeks after ligation of ureter the anastomosis between the dilated ureter and bladder was made by a double row of sutures. Cultures³ from dilated ureter, which contained bloody turbid fluid, showed *Staphylococcus albus*.

May 8, 1909. Doing well.

May 22, 1909. Nephrectomy (left kidney).

June, 1909. Dog did very well.

July 11, 1909. Sudden development of anuria followed by death.

Autopsy. Calculus found plugging the ureter. Kidney shows dilated pelvis full of white calculi, one of which had wandered into and blocked the ureter, producing the fatal anuria.

Remarks. In this dog the kidney had been excluded three weeks before it was allowed to resume its work, and after this period it was still capable of doing the necessary excretory work. No signs of renal insufficiency developed until the accidental blocking of the ureter by a calculus took place.

Experiment. (38). Fox terrier.

August 16, 1909. First operation. Ligation of right ureter close to bladder.

September 15, 1909. Anastomosis of ureter and bladder thirty days after the first operation. Cultures showed *Staphylococcus albus*.

December 13, 1909. In good condition.

February 19, 1910. Nephrectomy (left kidney).

February 20, 1910. Doing well.

Urinalysis. Specific gravity, 1030; alkaline reaction; faint trace of albumin; 2 per cent. urea; phosphates and pus cells.

³ I take this opportunity to thank Dr. H. Celler for the bacteriological examinations which he very kindly made for me.

February 21, 1910. Total urine gathered, 345 c.c.; specific gravity, 1020; alkaline; 1.5 per cent. urea.

February 22, 1910. Total urine gathered, 480 c.c.

February 23, 1910. Total urine gathered, 750 c.c.

February 27, 1910. Total urine gathered, 720 c.c.

March 5, 1910: Dog in excellent shape. Continues to take food well; no vomiting; active and growing fat.

March 19, 1910. In excellent condition.

April 8, 1910. Killed. Autopsy showed a large stone in bladder, three-quarters of an inch in diameter. New ostium patent. Right ureter somewhat dilated. Right kidney is approximately one-third the size of the previously excised left kidney, which had been removed February 19, 1910. It measures one inch in the vertical and one-half inch in transverse diameter.

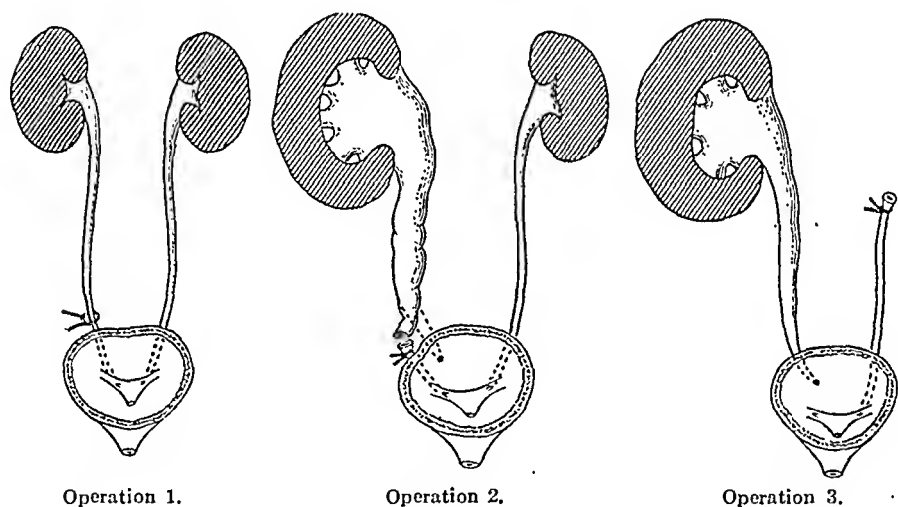


FIG. 8.—Series testing functional adequacy.

Remarks. This dog lived satisfactorily on the right kidney, which did all the necessary excretory work, even though it had been excluded for thirty days. In still another dog (Case 40) I excluded a kidney for thirty-seven days, and when it was tested by the same physiological test, that is, forced by nephrectomy of the second organ to do all the work, it excreted four days after the nephrectomy 650 c.c. of urine, which on testing was alkaline in reaction, contained a faint trace of albumin, urea 1.6 per cent. (10.4 grams). Subsequently this animal developed signs of insufficiency, and vomiting set in, followed by anuria and death.⁴

Resume. From such experimental data it is evident that even after three or four weeks exclusion of a kidney, sufficient parenchyma is preserved to carry on the excretory work of the organism. Whether these results in dogs can be transferred to humans,

⁴ Fig. 8 illustrates the various steps taken to test the adequacy of the excluded kidney.

experience alone can tell us. The knowledge gained from these data are very suggestive and in future if an operator resorts to ligation of a ureter, he must bear in mind the fact that the excluded kidney may be made a useful organ if an anastomosis is made within three to four weeks of the original exclusion.

From the work done in connection with this subject, the following conclusions seem justified:

1. Infection of a non-stenosed ureter may lead to a hydronephrosis. Perhaps this explains some of the cases of hydronephrosis in which no mechanical cause is found.

2. Infection of the ureter rarely leads to abscess formation, to multiple abscesses of kidney, unless the ureter is stenosed and then only when the injected organisms are virulent.

3. Aseptic ligation of ureter leads regularly to a primary hydroureter and at about three weeks atrophy and shrinkage of the hydronephrotic sac begins.

4. The idea that the use of catgut ligature material in pelvic work will not cause a permanent ureteral stenosis, if this organ is tied off, is erroneous.

5. Three to four months after ligation of the ureter the kidney is represented by a small fibrous mass, provided infection is not present. If infection is introduced a huge hydronephrotic sac without vestige of parenchyma results.

6. In face of infection, stones readily form both in the pelvis and bladder.

7. After three weeks' exclusion sufficient parenchyma persists to warrant an attempt at secondary implantation of the ureter into the bladder.

THE USE OF THE CREHORE MICROGRAPH IN THE CLINICAL AND EXPERIMENTAL STUDY OF CARDIOVASCULAR PHYSIOLOGY.¹

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(From the John Herr Musser Department of Research Medicine, University of Pennsylvania.)

In the last few months we have attempted to use the Crehore micrograph² for the study on animals of (1) the time relations of

¹ Read before the Philadelphia Pathological Society, May 9, 1912.

² AMER. JOUR. MED. SCI., 1912, cxliii, 193.

the contractions of various parts of the heart, (2) the correlation of these with intra-auricular and intra-ventricular pressures, (3) the transmission time of pulse waves under various conditions, and (4) the time relations of heart sounds and of murmurs. Clinically we have tried to apply it to the study of the jugular pulse, of heart sounds and murmurs, and of the transmission time of the pulse waves. It has been impossible to complete any phase of the work, because in the use of the instrument we have met with constant difficulties. These have been for the most part of a technical nature, which could be met by some modification of the construction or by a sufficiently frequent readjustment of the instrument, but which are so numerous that for their correction an almost complete reconstruction of the instrument would be necessary. In addition to these minor difficulties there are some objections to the principle of the Crehore micrograph when applied to physiological studies. Some of our difficulties were as follows:

1. *The Tambours.* We found that upon testing our tambours they were not air tight. To render them so it was necessary either to seal the joint between the base of the tambour and the diaphragm, forming its upper surface, or to place some form of washer between these two. The instrument not having been constructed with a view to this change, neither operation has proved to be altogether simple, and, in fact, we have found it difficult to so adjust the instrument that when a given displacement on the receiving tambour is made and maintained there will not be a gradual return of the recording tambour toward the resting position. Such a defect, of course, renders the instrument useless for graphic registration.

Another unfortunate feature of the instrument is in the mirrors attached to the tambours. These mirrors are but lightly silvered. If they be too little silvered, not enough light will be reflected to give a good photograph; if, on the other hand, they be too heavily silvered, the interference bands are obscured and the record cannot be read. As the silvering undergoes oxidation in the air resilvering must be done from time to time, and no method has yet been devised for securing precisely the correct degree of silvering except that of repeated trial.

The adjustment of the interference surfaces is likewise a time-consuming operation. Once the interference bands appear it is a matter of no difficulty whatever to adjust them properly, but it is often a matter of minutes or even an hour or more before they can be made to appear at all.

2. *The Photographing Apparatus.* One of the most serious difficulties which we have encountered is the inadequate provision for securing an evenly moving film. Whether soft copper wire be used to draw the film holder along its track or steel wire, which is less prone to kink, the movement of the film is far from even.

This is shown by the use of some type of time-marker, and also by the alternately darker and lighter zones across the film due to varying lengths of exposure as the rate of the film changes. Such a defect, of course, renders accurate time measurements impossible.

Another defect is the limitation in both directions as to the speed that can be chosen for the film. As noted above, the mirrors must not be too highly silvered or the bands will be obscured. This means that the intensity of the light reaching the film is limited, and in turn the rate of the moving film must be kept below a certain speed in order to secure sufficient exposure. On the other hand, if the film is propelled too slowly, the exposure is sufficient, but the bands at those parts of the record where their change of position is most rapid, fuse with each other in the photographic record, and, of course, cannot be interpreted. These difficulties would be lessened had the camera been constructed with an adjustable aperture which could be widened for rapid and narrowed for slow speeds, instead of with a fixed aperture. Even then, however, the margin between the two limits of speed would be small. As constructed the instrument lends itself, when the pulse rate is 70 per minute, to the recording of about one and one-half to three cardiac cycles. For most purposes, both clinical and experimental, however, a record as brief as this is not satisfactory. The film carrier should be constructed to take a record several times this length.

3. *Interpretation of the Photographic Record.* It is the interpretation of the photographic record itself, however, which presents the greatest difficulty. If at any point the movement of the bands has been so rapid as to cause them to blend, or if for any other reason the record is obscured at one point, the relation of the bands to each other on the two sides of this point cannot be determined. In addition to this, the impossibility, in experimental work, of using the machine for fluid transmission of pulse waves instead of for air transmission, is often a serious defect. Still more serious is the fact that a base line cannot be established.

Finally, very minute waves are at times present. These average about 250 to the second, are of very small amplitude, and sometimes can be shown to be artifacts, due to vibrations in the instrument. The plotting of these minute waves is most arduous, yet if the investigator assume the right to plot them or not, as he sees fit, an opportunity for subjective error is at once introduced. This is particularly true in the study of murmurs and heart sounds, and the smaller waves of the pulse. It is, however, the study of these sound waves and smaller waves of the pulse, which is the chief excuse for the use of an instrument of such great sensitiveness as the Crehore micrograph, but in this, unfortunately, it fails. The importance of the study of these smaller waves and of the time relations of the sound waves of the heart to the phases of the cardiac

cycle is suggested by Frank's³ work with his mirror manometer, as also by Veiel,⁴ Müller and Weiss,⁵ Weber and Wirth⁶ with the same instrument, and by the work of Einthoven and others with the string galvanometer.

In conclusion let us point out that the Crehore micrograph, even if free from technical defects, has no advantages not offered by the mirror manometer of Frank. Moreover, the latter is an exceedingly simple apparatus to operate, is apparently as sensitive to the small waves of the pulse and to sound waves as is the Crehore micrograph, if not more so, gives a photographic record that does not have to be plotted, but can be published directly, and if for any reason the record is defective at one point, this in no way impairs the interpretation of the other parts of the record. Furthermore, a base line is readily established and the instrument lends itself to water transmission of impulses as well as to air transmission.

³ *Zeit. f. Biol.*, 1904-05, xlv, 441.

⁵ *Ibid.*, 1912, cv, 320.

⁴ *Deut. Arch. f. klin. Med.*, 1912, cv, 249.

⁶ *Ibid.*, 1912, cv, 562

REVIEWS

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia, etc. Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, etc. Vol. I, pp. 377; 7 illustrations. Philadelphia and New York: Lea & Febiger, March, 1912.

THE first volume of *Progressive Medicine* for this year has recently appeared. The opening section of 101 pages by Charles H. Frazier is an excellent critical review of the surgery of the head, neck, and thorax. He first takes up the brain and under this heading describes, along with other interesting topics, the hypophysis, cerebral decompression, brain puncture, hydrocephalus, brain tumors, and cranial fractures. After he covers comprehensively the mouth, face, jaw, and neck, he devotes 18 pages to a consideration of the thyroid gland, the parathyroids, and the thymus. Under thoracic surgery Frazier discusses the mammary gland; the heart and pericardium; intratracheal sufflation, over which he is justly enthusiastic; empyema; the surgical treatment of pulmonary tuberculosis, and other phases of the surgery of the lungs and the esophagus.

John Ruhräh has contributed, as usual, an admirable review of the extensive literature on infectious diseases that has appeared during the last year. It is out of the question to attempt to enumerate in detail the wealth of interesting material discussed in this contribution of 144 pages. Among some of the subjects to which particular attention has been paid, may be mentioned Brill's disease, cholera, diphtheria, hookworm disease, malaria, Malta fever, the work of Anderson and Goldberger on experimental measles in the monkey, pellagra, poliomyelitis, scarlet fever, and smallpox. In addition, however, Ruhräh has entered into the always important subjects of tuberculosis and typhoid fever with unusual thoroughness, devoting 35 pages to their consideration.

Diseases of children are covered in 32 pages by Floyd M. Crandall, who emphasizes in particular hemorrhagic diseases of infants, the urine and purulent infections of the urinary tract in infants, indi-

gestion in older children and gastric disorders in infants, and concludes with a discussion of infant foods and artificial feeding.

The last 89 pages of this volume are devoted to a contribution by D. Braden Kyle of 52 pages on rhinology and laryngology and one on otology by Arthur B. Duel. Kyle lays particular stress upon vasomotor disturbances of the nose, common colds, the ocular symptoms and other complications of sinus disease, the tonsils, cancer of the larynx, and the treatment of stuttering. The major portion of Duel's article is taken up with a discussion of syphilis, otosclerosis, diseases of the labyrinth, and the organs of hearing and multiple sclerosis.

A survey of the interesting and carefully compiled information contained in Vol. I makes it evident that during 1912, as heretofore, *Progressive Medicine* must be accorded first rank among current works of reference.

G. M. P.

THE SENSIBILITY OF THE ALIMENTARY CANAL. By ARTHUR F. HERTZ, M.A., M.D., F.R.C.P. Pp. 83. London: Henry Frowde and Hodder & Stoughton, 1911.

UNDER this title were delivered the Goulstonian Lectures at the Royal College of Physicians, in March of 1911. The experimental work forming the foundation of this publication was undertaken with the object of interpreting pathological sensations in the alimentary tract, on the basis of disturbance of sensibility of healthy organs. With this object in mind, various divisions of the digestive apparatus have been studiously investigated as to their reaction to tactile, thermal, and chemical stimuli, and on what depend the sensations of fulness and distention, the sensations of emptiness and hunger, and the sensation of pain.

There has been a great deal of experimental work devoted to this study of Dr. Hertz, and we congratulate him on the zeal with which he has attacked the subject, and on the interesting way in which he offers his results to our critical eye. The original lectures have been slightly changed in order to bring the reading matter into a chapteral arrangement. Although the author's trend of thought is easily followed, the impression of facts gathered is reinforced by a very concise summary or *resume* at the close of certain chapters, and at the end of the book by a most contracted list of conclusions.

The chapter on pain has interested the reviewer the most.

Having reviewed for this JOURNAL about a year ago, the book by Mackenzic on *Symptoms*, the writer was interested in noting the divergent view of Hertz from that of Mackenzic on the cause

of visceral pain. The former's credo is tersely expressed in the following words: "I believe that tension is the only cause of true visceral pain," while the latter's theory is based on the production of the viscerosensory reflex. In this chapter, on page 57, appears this sentence: "The contact of free hydrochloric acid with the intact mucous membrane, and with the surface of an ulcer, does not itself cause pain," while on page 58 appears this: "Consequently an hour or more may pass before there is sufficient free acid to irritate an ulcer near the pylorus." Later: "An ulcer in this (intermediate portion of the stomach) situation, is irritated by acid at an interval after a meal," etc. Several readings of parts of the book calculated to clear up this apparent contradiction were productive of no enlightenment of the reviewer's confusion.

The work is interesting, and being mostly original, the opinion regarding it should be conservative until more work has been done along similar lines by other investigators.

E. H. G.

TEXT-BOOK OF PATHOLOGY. By FRANCIS DELAFIELD, M.D., LL.D., Emeritus Professor of the Practice of Medicine, College of Physicians and Surgeons, Columbia University, and T. MITCHELL PRUDDEN, M.D., LL.D., Emeritus Professor of Pathology, College of Physicians and Surgeons, Columbia University, New York. Ninth edition. Pp. 1114; 13 full-page plates; 687 illustrations. New York: William Wood & Co., 1911.

THE latest edition of this well-known work has been considerably extended both by additions to the text and by the insertion of over forty new illustrations which are well chosen and add much to the value of the work. Part first, dealing with general pathology, has been rewritten and expanded. The chapter on inflammation is clear and includes complete directions for the experimental demonstration of the phenomena of inflammation. To the chapter on immunity has been added a section on anaphylaxis and one on the technique of the common serological procedures; that of the Wassermann reaction is added to the section on syphilis. The extensive use of the term "alexin" for the now almost universally accepted term "complement" seems unfortunate. Stains for *treponema pallidum* and for Negri bodies are described. A new chapter on the common malformations, well illustrated, has been introduced. The chapter on tumors has been rewritten. The descriptions of the various tumors is necessarily brief; that of chorionepithelioma, with illustrations, has been added. In outlining the theories of tumor production Ribbert's, in its recently modified form, is emphasized rather more strongly than the others.

A section on tumor transplantation has been added and references cited as recently as 1910.

In part second, dealing with special pathology, the physiological determination of the alkalinity of the blood and the significance of leukocytic ferments are considered. The leukemias and Hodgkin's disease have been rewritten; the latter is particularly complete and well illustrated. The ductless glands receive only brief mention. In discussing fatty degeneration of the liver the authors still hold to the old view now discarded by many pathologists that the fat is formed by a retrograde metamorphosis of the proteid elements of the protoplasm. Mention is made of Opie's production of experimental acute yellow atrophy, and also briefly of the various attempts to produce experimental cirrhosis. The discussion of nephritis has not been altered, but is an exceedingly clear exposition of the subject; the difficulty of correlating the pathological and the clinical types is recognized.

Part third, devoted to autopsy technique and to the preservation and study of tissues, is practically unaltered except for the addition of three illustrations showing the method of opening the heart. This section of the book is brief, but sufficiently detailed to be of value to the student. The references to the literature throughout the book are well chosen and are most valuable. They are selected especially with a view to the bibliographies they contain. They are cited as recently as 1910 (in one instance 1911), on those subjects on which work has been recently done. The index is good and includes an authors' index of all references cited. The authors are to be congratulated upon the marked improvements made in a work already one of the standard text-books on its subject.

J. H. A.

LEHRBUCH DER KYSTOSKOPIE UND STEREOKYSTOPHOTOGRAPHISHER ATLAS. By DR. S. JACOBY, Ehemalig. I. Assistenten von Weiland Geh. Mediz.-rat und A. O. PROF. DR. MAX NITZE an der Universität in Berlin. Pp. 247; 48 stereoscopic plates and 121 illustrations in the text. Leipzig: Werner Klinkhardt, 1911.

THE text occupies 247 pages, and its arrangement is similar to that of other standard works on the same subject. The first four chapters contain a description of cystoscopy construction, including the original Nitze instrument and its numerous modifications. Minute instruction is given in cystoscopic technique, the care of instruments, and the various procedures of an examination, with methods of overcoming difficulties that may present themselves. Exclusive of an excellent chapter dealing with the anatomy and physiology of the bladder and urethra, twenty-seven pages are

devoted to the normal bladder as seen through the cystoscope; normal variations, important landmarks, methods of locating the ureteral orifices, etc., are fully and accurately detailed. The author has succeeded admirably in presenting a vivid description of the pictures observed in the various pathological conditions of the bladder, including not only the common but the rare diseases as well. The technique of ureteral catheterization with its diagnostic importance, pyelography, functional kidney diagnosis, and the possibilities of intravesical treatment by means of the cystoscope are given in detail. The concluding chapter deals with a description of the photographic cystoscope, its mechanism and methods of employment. The forty-eight stereoscopic photographs are attractively presented and remarkably clear but the absence of color detracts greatly from their usefulness in conveying to the reader the actual conditions as viewed through the cystoscope. The author has covered the entire field of cystoscopy in a thorough, scientific, and up-to-date manner which places his book among the best on this important specialty. F. E. K.

TEXT-BOOK OF EMBRYOLOGY. By FREDERICK R. BAILEY, A.M., M.D., formerly Adjunct Professor of Histology and Embryology, and ADAM M. MILLER, A.M., Instructor in Anatomy, College of Physicians and Surgeons (Medical Department of Columbia University). Second edition. Pp. 672; 515 illustrations. New York: William Wood & Co., 1911.

THE book represents the outcome of the authors' practical experience in conducting laboratory courses in embryology for medical students, and is, therefore, intended especially for that class of men. The subject is treated in two parts—general development and organogenesis. Under Part I are considered the structure of the cell and cell division; the sex cells, their maturation and fertilization; segmentation of the fertilized ovum; the formation of the germ layers; fetal membranes and the development of the external form of the body. Under Part II is taken up the normal development of the various systems and organs of the body, with a final chapter on teratogenesis. Each chapter is followed by practical suggestions giving the technique for the study of the subjects treated in that chapter, and by the list of references to original papers for further study. In an appendix is given the more general microscopic technique, and the volume ends with an index of thirty-three pages. The book is well printed on heavy paper, with large clear type. The illustrations are numerous, and are reproduced for the most part from other sources, the remainder being from photomicrographs.

The primary object of the authors was to present to the student of medicine the most important facts of development, at the same time emphasizing those features which bear directly on other branches of medicine. Considering the nature of the subject and the time allowed for its study in the medical school curriculum, their purpose has been well achieved. In such a course of instruction it is impossible to present all parts of the subject equally fully. For instance, when one considers the magnitude of the subject of cytology at the present time, it is easily realized how little of this must suffice for the student after he has entered the medical school. Luckily for the present day student he is learning more and more of the fundamental processes of embryology in his premedical days in courses on the frog and the chick, and this allows more time and gives him better preparation for the study of the histogenesis of the mammalian organs. The portion of the volume devoted to the latter subject is particularly interesting in that it shows in the practical suggestions offered the amount of human material which may be utilized in class teaching. Nowadays more physicians are awake to the value of all stages of the human fetus to the teacher of embryology, and in consequence more of this material is saved, preserved in some convenient fluid, such as 10 per cent. formalin, and turned over to a laboratory.

The obvious criticism is that the authors have attempted to cover too much ground, using all classes of the animal kingdom for their illustrations, but until all students have complete courses in comparative embryology before entering medicine this method of teaching must continue.

Such volumes as this show that embryology is no longer an abstract science, to be learned through charts and diagrams, but one which, like normal and pathological histology, may be demonstrated on actual tissues.

W. H. F. A.

ANESTHESIA AND ANALGESIA. By J. D. MORTIMER, M.B. (Lond.), F.R.C.S., Eng. Anesthetist of Royal Waterloo Hospital; Throat Hospital of Golden Square; St. Peter's Hospital for Stone; Instructor Medical Graduate College. Pp. 276; 29 illustrations. London: Hodder and Stoughton and Henry Frowde, 1911.

As the author states this work is in the form of a manual for the general practitioner and student and is essentially a practical treatise. In it no attempt has been made to consider the chemical properties, the history, or the theories concerned in the action of the various drugs used. No mention is made of the more modern

methods that are still on trial and have not as yet been definitely proved safe. Nor is anything said of those methods demanding complicated apparatus and which are used almost exclusively by the specialist.

The care of the patient before and after the anesthesia, the duties and the responsibilities of the anesthetist, and the method of administration of the drug are all described in the fullest detail. Each sign and symptom that might arise is described and the remedial measure given.

Each anesthetic is then discussed separately with the method of its administration, its advantages, indications, and contraindications. The author contends after a large experience that an anesthetist should, in each case, consult with the surgeon and choose that anesthesia which will best suit the individual, both as far as the immediate and the remote complications or sequels are concerned.

An interesting and instructive feature of the book is the chapter on the medicolegal position of the anesthetist. The book is of a handy size, but its binding and paper render it rather difficult to leaf over. In one or two instances the illustrations fall short of what could be desired in a work of this type. E. L. E.

A PRACTICAL GUIDE TO THE NEWER REMEDIES. By J. M. FORTESCUE-BRICKDALE, M.A., M.D., Oxon., Lecturer on Pharmacology in the University of Oxford. Pp., 273. New York: William Wood and Co.

THIS little book fills a gap in the practitioner's office library that will prove of considerable value. It takes up in detail the relative merits of a large number of preparations, many of which are known under proprietary or trade names and yet which are neither patent medicines nor secret remedies, concerning whose efficacy and reliability the busy doctor may be skeptical. The information given concerning these less well-known drugs if properly studied will serve to augment our armamentarium.

A good feature of the book lies in the clearness with which the various classes of drugs are compared one with the other, and for and against whose usefulness all the clinical and experimental evidence (with numerous references to the original literature) has been adduced; and in addition the author expresses his own views as to which drug or drugs in each group has been proved most worthy of confidence.

The scope of the book, while not exhaustive, is sufficiently large. As the author states in his preface and introduction, his object is merely "to pass in review the newer drugs (mainly the result of

synthetic chemistry) the composition of which is published and whose pharmacology has been more or less accurately ascertained, give some account of the properties and dosage of the principal drugs in each class, and to indicate their relative and collective value as accurately as possible by reference to clinical experience, laboratory experiment, and a study of the literature." This the author has admirably succeeded in doing, and in a very practical manner, eliminating as far as possible a too detailed discussion of the more intricate theories of chemistry. He has wisely excluded the animal group of drugs, as well as a consideration of serum and vaccine preparations. In regard to the arsenical group, it is, perhaps, to be regretted that the book was published too early to admit of a review and discussion of the merits of salvarsan.

Among the several excellent chapters, the one devoted to an impartial discussion of the drugs making up the spinal anæsthetic group is especially to be commended. V. L.

HANDBOOK OF MEDICAL TREATMENT. A GUIDE TO THERAPEUTICS FOR STUDENTS AND PRACTITIONERS. WITH AN APPENDIX ON DIET. By JAMES BURNET, M.A., M.R.C.P. (Edin.), etc. New York: William Wood & Co., 1911.

THIS little pocket handbook consists of a brief outline of treatment of all medical and dermatological conditions, of some neurological, and a few surgical conditions. In addition, there is an appendix on diet, including infant food. The advice is logical and clearly given, but necessarily extremely brief. The value of such a book is very questionable. In the title the author says the book is a guide for students and practitioners. A student carefully and conscientiously trained at a good medical school has no use for such a book; while in the practitioner it encourages the employment of superficial and careless methods of dealing with cases to consult for advice a book which disposes of the large subject of therapeutics in such a concise and limited manner.

J. H. M., JR.

FORTPFLANZUNG VERERBUNG RASSENHYGIENE. By PROF. MAX V. GRUBER and PRIV. DOZ. DR. ERNST RÜDIN. Pp. 178; 230 illustrations. Munich: J. F. Lehmanns, 1911.

A CATALOGUE of rest and hygiene presented in Dresden in 1911 at the International Hygiene Congress. T. H. W.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Rapid Method of Diagnosticating Hypercholesterinemia by Means of Saponin.—L. BOIDIN and CH. FLANDIN (*Compt. rend. Soc. de biol.*, Paris, 1912, lxxii, No. 1, 28) find that eholesterin prevents hemolysis by certain hemolytic agents, notably saponin. Boidin and Flandin have made use of this fact in testing blood serum for an excessive eholesterin content. Saponin, the serum to be tested, and washed eorpuseles are mixed in certain stated porportions so that, normally, hemolysis will occur at room temperature immediately; within five minutes, completely, partially; or not at all. Thus in a given case it can be stated whether the eholesterin content of the serum to be studied is higher or markedly higher than normal. Boidin and Flandin have never seen a case of marked cholesterinemia not having this power to prevent hemolysis under such conditions, nor any case in which the antihemolytic power was marked which did not show excessive eholesterinemia. Such sera may appear normal, or be derived from jaundiced or lactating patients. They have found that neither of these conditions are necessarily accompanied by hypereholesterinemia. In conclusion Boidin and Flandin claim that the procedure is simple and rapid. It is not delicate, only emphasizing marked cases, without reference to hypocholesterinemia. But in a suspected case this method makes it possible to tell clinically and at once, if the serum is markedly hypereholesterinated.

A Stain for Spirochetes.—T. SHAMAMINE (*Zentralbl. f. Bakt., Parasitenk. u. Infektionskr.*, 1911, lxi, 410) proposes the following technique for the staining of spirochetes. With it he obtains satisfactory stains

of *Spirochete pallida*, even from cultures. (1) Fixation of the preparation in the flame or, better, in methyl alcohol. (2) Place three or four drops of 1 per cent. potassium hydrate on the smear. (3) Add immediately to this several drops of fuchsin solution ("fuchsin, 15 grams; 96 per cent. alcohol;" dilute one part of this with twenty parts of water) or of concentrated aqueous solution of crystal violet. (4) Allow this mixture to act about three minutes; the stain becomes cloudy and a precipitate appears; finally the fluid becomes decolorized. (5) Wash in water, dry, and mount in balsam. If one desires more intense staining, the specimen may be restained two or three times. With crystal violet better results are secured by substituting 4 or 5 per cent. sodium carbonate solution for the sodium hydrate.

Some Points in the Diagnosis and Treatment of Chronic Duodenal Ulcer.—B. G. A. MOYNIHAN (*Lancet*, 1912, clxxxii, 4610, 9), in the diagnosis of duodenal ulcer, emphasizes the importance of a careful history. It has been stated that the picture of disease thus established does not differ notably from that which has been recognized for generations as hyperchlorhydria. Moynihan believes that this is a term to be used strictly to indicate an excess of active HCl in the stomach contents. It is present in most cases of duodenal ulcer during the active stage of ulceration—hence its importance in this disease as an aid to diagnosis—but is found in other diseases, notably appendicitis and cholelithiasis. The persistent presence of an excess of active HCl in the stomach contents is indicative of an organic rather than a functional disorder. X-ray examination after a meal of bismuth, with milk, or bread and milk, in uncomplicated cases of ulcer, affords a most striking spectacle. The activity of the stomach is greatly increased, food beginning to pass into the duodenum at once, and continuing with greater rapidity than normal. By the time the pain begins to appear, the stomach is nearly empty, and most of the bismuth has left the duodenum. In cases of active ulceration, a daily examination of the stools will reveal the frequent if not constant presence of blood. Physical examination is only of the slightest value until obstruction develops. The surgical treatment of chronic duodenal ulcer in the majority of cases is gastroenterostomy. Since both perforation and hemorrhage have occurred many weeks or months after the apparently successful operation, Moynihan considers local treatment essential, best carried out by infolding of the ulcer. Moynihan thinks that diseases of the stomach duodenum, and gall-bladder are secondary, due to a primary infection or toxemia originating in some abdominal organ. In many cases the appendix is diseased, though other sources are possible. Hence routine examination of the abdomen is indicated, as development of jejunal or gastrojejunal ulcer close to the anastomosis may be determined by the continuance of the original source of infection if undiscovered.

A Stain for Diphtheria Bacilli.—MARIE RASKIN (*Deutsch. med. Woch.*, 1911, xxxvii, 2384) has devised a new stain for the demonstration of *B. diphtheriæ*. The mixture consists of: Glacial acetic acid, 5 c.c.; distilled water, 95 c.c.; alcohol, 95 per cent., 100 c.c.; old saturated aqueous solution of methylene blue, 4 c.c.; Ziehl's carbol-fuchsin, 4 c.c.; This mixture is spread over the preparation in a thin layer and drawn

through the flame. The alcohol ignites and burns in eight to ten seconds. After the stain is allowed to act five to six seconds longer, it is washed off with water, the specimen blotted dry, and examined. The polar granules are stained deep blue, the bodies of the bacilli bright red. Even when diphtheria bacilli are few in number in a mixed culture, they are readily seen. The whole procedure requires only twenty to twenty-five seconds. The stain may be kept indefinitely.

Nitroglycerine Poisoning.—R. READ PIRRIE (*Practitioner*, 1912, xii, 259) considers the history of nitroglycerine, its method of manufacture, its pharmacological and physiological action, emphasizing the fact that individual susceptibility in poisoning plays an important role. Among workers with the drug, there is a general opinion that it can be absorbed through the intact skin. Some miners are very cautious in handling explosives, other reckless. All nitroglycerine compounds are liable to become frozen at 40° F., and require a temperature of 50° to soften them. When the weather is cold, some miners have "warming pans" for thawing the explosive; others place it next to the bare skin so soon as they enter the pit, when the body heat softens it and renders it in a condition to be worked by the hands into a shape suitable for use. In imperfect explosion carbonic acid, carbon monoxide, and volatilized nitroglycerine may be given off. Thus workers, by absorption or inhalation may be exposed to poisoning. Pirrie reports 7 cases among explosive workers. They complained of varying acute symptoms, especially headache, vomiting, and jaundice in certain cases. There was one case of optic atrophy, analogous, Pirrie believes, to the enlargement of retinal vessels, with blurring of the disk, found in certain dinitrobenzol workers. There was one death. Autopsy was negative save for dark-colored blood. Pirrie concludes that on account of its volatile character, it is difficult to detect the poison chemically. That workers with nitroglycerin are liable to acute poisoning, the effects of which are neither dangerous to life, nor of long duration. The possibility of change in the retina and optic nerve may be important. For prophylaxis he advises greater care in handling the explosive, and freer ventilation. For treatment of the acute symptoms, fresh air and oxygen inhalations if necessary.

The Passage of Hemoglobin through the Kidneys.—WARRINGTON YORKE (*Annals of Tropical Medicine and Parasitology*, 1911, v, series 7 M., 401) has found that if an isotonic solution of hemoglobin obtained from rabbits' red blood corpuscles was injected into a vein of a normal rabbit, the urine a few minutes later was tinged with hemoglobin. The injection of large amounts under certain conditions caused suppression. The degree of hemoglobinuria did not reach its maximum for several hours after injection, nor did it parallel the hemoglobinemia. Thus, when several large amounts of hemoglobin were injected at stated intervals, the hemoglobinuria resulting from the last injection was usually much less than that following the first, even though at the end the hemoglobinemia was greater. Microscopic examination of such kidneys showed occlusion of the tubules by casts of varying appearance, according as the tissue examined was obtained from animals which succumbed shortly or later after injection. In the early stages,

the casts were found limited to the cortical tubulcs, not involving Bowman's capsules. They were slightly granular, appearing to consist of a fairly homogeneous material staining like blood. In the later stages, in addition, casts were found in the larger tubules, were much more granular, and in part crystalline. Yorke believes that such were undoubtedly derived from hemoglobin, though not giving a staining reaction for iron. Comparable lesions are found in kidneys of dogs infected with *Piroplasma canis*, and in human kidneys from patients with blackwater fever and suppression of urine. On the whole, Yorke concludes that hemoglobin is secreted by the epithelium of the convoluted tubules, and the amount eliminated is dependent on its activity.

Human Infection with *Tænia Cucumerina*.—J. LINS (*Wien. klin. Woch.*, 1911, xxiv, 1595) reports 6 cases of infection of man with *Tænia cucumerina* (*Dipylidium caninum*). This parasite is the commonest tape-worm of dogs; it is not infrequent in cats, but rare in man. Only 60 cases of human infection had been recorded previously. Most of the cases have occurred in children two years of age (36), between two and five years there have been 15 cases, 2 cases between nine and twenty years, and only 6 cases in adults (over twenty years). In only 15 instances was more than one worm found. In one of Lins' cases more than 208 intact parasites were passed following treatment; this is the largest number reported. The patient was a woman, aged thirty-eight years. Four of her children were infected with the same parasite. The remaining patient was a woman, aged twenty-nine years. In all 6 cases multiple infections were found.

The Determination of Individual Dosage in Tuberculin Therapy.—WILLIAM CHARLES WHITE and KARL H. VAN NORMAN (*Arch. Int. Med.*, 1912, i, 114) describe again a method by which they determine the sensitiveness of an individual to tuberculin by using on the skin a definite quantity of varying dilutions of tuberculin; then having arrived at the dilution which with a given technique will give a minimal cutaneous reaction around the point of scarification, to determine on this basis the quantity of tuberculin of the same strain, which can be given for therapeutic purposes, intrautaneously to produce a reaction of required degree. As there is no possibility of grading the dosage according to the extent of the disease, by this method it is possible to produce the same grade of reaction in any given number of patients. As patients vary in sensitiveness, and as in a few cases it has been found that increasing doses may be given every two weeks with the same or diminishing local reaction as obtained formerly on the minimal cutaneous reaction basis, the dose should be confirmed every three months by a repeated skin test. White and Van Norman believe that tuberculin should be given in only those cases where the maximum temperature does not exceed 99.6°; to patients who are fairly nourished, and whose general outlook seems favorable. In such by the method described, they find that the patients improve much more than when tuberculin is given with the desire of producing tolerance, the patients feeling better, coughing less, and being better able to stand exercise and strain.

SURGERY

 UNDER THE CHARGE OF

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Intracranial Path to the Hypophysis Cerebri through the Anterior Cranial Fossa.—BOGOJAWLENSKY (*Zentralbl. f. Chir.*, 1912, xxxix, 209) says that the question of the best approach to the pituitary body is not yet decided. According to the figures of Melchior, in 39 cases operated on, the transnasal path of Scloffer was employed with some modifications. Besides the technical difficulties of the work, at a depth of 8 to 10 cm., without any control of the eyes, it is impossible to do the operation aseptically. At the best only a part of the sella turcica can be removed, while the hyperplastically changed hypophysis with the tumor in it, usually extends beyond the limits of the sella turcica. One would expect that the intracranial path would have attracted more attention from the surgeon, but all reported cases which have been performed by this route, either failed or were not completely successful. Above all the approach through the middle fossa, by elevation of the temporal lobe of the brain, will not succeed, because it becomes indispensable to lift very strongly on the brain so that serious damage is unavoidable. It is also difficult to avoid damage to the sinus cavernosus. The path through the anterior fossa avoids these dangers. Two cases were found in the literature in which the operation was done through the anterior fossa. In the first, that of Arthur, the sella turcica was exposed by a two-sided broad craniotomy and elevation of the frontal portion of brain on both sides. Death occurred some hours after the operation. In the second case, that of F. Krause, the intracranial approach was from the right frontal region. Although this patient recovered, the operation which was performed for a sarcoma of the hypophysis accompanied by a bilateral optic atrophy, was followed by a paralysis of the left facial nerve and the left extremities. Bogojawlensky reports the following case: A man, aged thirty-five years, began to complain two years before of a severe headache which was soon continuous and so severe that he became bed-ridden, and for one and one-half years could not sit up. The signs of acromegaly were present. The operation was performed in two stages. In the first an osteoplastic flap, 9 cm. high and as wide, was lifted, its medial border being $2\frac{1}{2}$ cm., from the median line and the lower border $2\frac{1}{2}$ cm. from the upper border of the orbit. One to $1\frac{1}{2}$ cm. of the bony margins of the opening in the skull was removed by

forceps, and with this the operation ended. The second stage of the operation was carried out six weeks later. After elevating the osteoplastic flap, the dura was opened by a H-shaped incision and the flaps turned upward and downward. The head of the patient was then brought over the edge of the table and the right frontal lobe of the brain was separated from the orbital roof, slowly and carefully, first with the finger and then with the Krause brain elevator. This gave a cleft, 5 cm. broad anteriorly, more narrow posteriorly. At a depth of about $7\frac{1}{2}$ to 8 cm., the right optic nerve was visible. A copious escape of cerebrospinal fluid prevented further examination. Raising the head end of the table about 30 degrees stopped this. Just in front of the optic commissure could be seen a dark red tumor which was tongue-shaped. It was removed with a curette which went to the bottom of the sella turcica without difficulty. The bleeding was slight. The dural flaps were sutured, the osteoplastic flap placed in position and the skin sutured. The postoperative course was without disturbance and the eyes were not affected. Three weeks later the symptoms of acromegaly began to disappear. Bogojawlensky considers that the intracranial route through the anterior fossa is not only the best, but the only method by which one can be completely aseptic and remove everything from the sella turcica under the control of the eyes, without injuring the brain or the optic nerves. It is necessary to employ artificial light, best in the form of an electric lamp with a reflector on the brow. The best position of the patient is obtained by elevating the end of the table to an angle of 30 degrees, with the head strongly retroflexed.

Nerve Anesthesia in Kidney Operations and Thoracoplasty and in Operations on the Trunk in General.—KAPPIS (*Zentralbl. f. Chir.*, 1912, xxxix, 249) says that novocain-suprarenalin gives us a relatively safe and strong local anesthesia. It is an important advance, particularly when peripheral nerve trunks are injected. It has been employed in operations on the trigeminus region and the extremities. Nephrotomy, amputation of the breast, and thoracoplasty have been done with it. Kappis has used it for a pyelotomy, a nephrolithotomy, and a nephrectomy. The method is as follows: In order to inject the intervertebral nerve, the needle is introduced about $3\frac{1}{2}$ cm. from the midline on a level with the lower border of a rib. The rib in this position is not palpable, but its position can be determined in the following manner. Even in stout individuals somewhere in the back, one of the lower ribs will almost always be palpable. The lower edge projects toward the median line. The needle is to be introduced at a point where the lower edge of the rib is $3\frac{1}{2}$ cm. from the median line. The rib is reached at a depth of about 4 or 5 cm., about in the angle between the transverse process and the rib, which can occasionally be distinctly felt. Keeping as much as possible in this angle at the lower border of the rib, the needle is pushed forward and somewhat medially, and the fluid divided between the level of the rib and $1\frac{1}{2}$ cm. deeper. When the injection has been made under one rib, the other points of injection are easily selected, since one simply keeps in the line $3\frac{1}{2}$ cm. from the median line and goes about 3 cm. upward or downward, seeking in a similar manner the lower edge of the rib and making the

injection. The transverse process of the lumbar vertebræ must always answer for the ribs, but they are further apart than the ribs. Ten cubic centimeters of a 1.5 per cent. novocain-suprarenalin solution is injected. The operation should begin in about a quarter of an hour after the injection. In his first two kidney operations, Kappis injected from the ninth dorsal to the second lumbar vertebra on the affected side. Since the stripping off of the peritoneum was not completely painless, in the next operation, he injected also the seventh and eighth dorsal, but without a better result. With a proper injection, the skin, soft tissues, and kidneys with a large portion of the ureter, will be completely painless, but not so with the stripping of the peritoneum. For this reason he has on one occasion given 15 drops and on another occasion 30 drops of ether. The method is an important advance in kidney operations, especially when the kidney not operated on is diseased. It permits the avoidance of a postoperative nephritis from the narcosis in the remaining kidney after a nephrectomy.

The Technique of Local Anesthesia in Thoracoplasty.—SCHUMACHER (*Zentralbl. f. Chir.*, 1912, xxxix, 252) says that Sauerbruch employed the following method in 35 cases of extensive rib resections: Small doses of morphine or of pantothon were given one hour before the operation. A 0.5 per cent. novocain solution with the addition of suprarenalin was employed, the solution being made freshly for each operation. According to the extent of the operation, from 10 to 200 c.c. were necessary. The line of the intended incision was first injected subcutaneously. From this anesthetic line the deeper tissues, chiefly the nerves, were injected. The needle was directed from below and inward, upward, and outward against the rib lying over the point of injection in the region of the angle of the rib. When the needle scraped the bone, 1 to 2 c.c. were injected. Then feeling for the lower border of the rib, 5 to 8 c.c. were deposited. At the costal angle the intercostal nerve passes from the middle of the intercostal space upward to the lower border of the rib above. The intercostal veins are already in the groove under the rib above. The injection is made for each rib to be resected. The first intercostal nerve under the first rib is injected successfully in thin patients, but less so in stout patients. For the axillary incision a large injection needle is passed as far as possible posteriorly along the convex border of the rib with continuous injection. In 20 out of the 35 operations, in which 4 to 8 ribs were resected, no chloroform was necessary. In the others a few drops were necessary to induce a partial, light narcosis. No accidents, such as penetration of large vessels, the pleura or lungs, were observed.

Parathyroids and Their Surgical Relation to Goitre.—MAYO and McGRATH (*Annals of Surgery*, lv, 185) say that numerous hypotheses, erroneous deductions, and illogical conclusions have been drawn in connection with the action of the parathyroids, but that there no longer seems to be substantial grounds for doubting the etiological relationship between them and one disease, namely, tetany. Experimental tetany has been produced in animals by the removal of parathyroid tissue, and experimental tetany may be reckoned, in a certain sense, tetany following operation upon the human thyroid gland.

Spontaneous tetany is caused by an hypoplasia with resultant insufficiency of the parathyroids. Pathological examinations seem to have proved that hemorrhages into the parathyroids have a positive significance in the causation of tetany, especially in childhood, and that these hemorrhages produce their effect by injuring the parathyroidal tissue, inhibiting its development and consequently decreasing its functional power. According to MacCallum and Ovegtlin all violent symptoms produced by parathyroidectomy—muscular twitching and rigidity, tachypnea, fibrillary tremors, increased rapidity of the heart beat, etc.—may be almost instantly cured by the intravenous injection of a solution of a calcium salt. The acetate or lactate in a 5 per cent. solution is usually employed. The condition of relief following the administration of these various salts lasts for perhaps twenty-four hours, when tetany may reappear. Analysis of the blood taken from a dog during tetany shows a calcium content which is only about half that of the normal dog on the same diet. Insufficiency of the parathyroids seems to be necessary for the production of tetany. Gastro-intestinal disease may be a contributing factor by causing a hypofunction of the parathyroids, which is the most frequent form of tetany, especially in children. Remembering the variable size, location, and appearance of the parathyroids, the surgeon should preserve all, especially gland-like, masses about the capsule in cases of operation on the thyroid gland. If such a mass be accidentally removed in the course of operation, it should at once be implanted beneath some part of the remaining capsule. According to Vincent and Jolly, the parathyroids left behind after thyroidectomy can, under conditions, develop in the direction of thyroid tissue, and a functional replacement also can take place. The ideal treatment of tetany would be to compensate for the glandular deficiency by transplanting parathyroids from other individuals, feeding with animal glands, the use of serum or the extract of parathyroid tissue. Unfortunately, none of these procedures has given dependable results. No reliable treatment is at present known.

THERAPEUTICS

UNDER THE CHARGE OF

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Transfusion of Blood for Typhoid Hemorrhage.—Booth (*Yale Med. Jour.*, 1912, xviii, 214) reports a severe case of typhoid that was complicated by hemorrhages. The use of the ordinary therapeutic procedures such as hypodermoclysis, injections of rabbit and human serum, and the administration of calcium lactate apparently had no marked benefit. The condition of the patient was so bad that transfusion of blood was done as a last resort. The effect of this was remark-

able, the temperature that was subnormal, rose to normal, and the pulse rate dropped to the same level that preceded the hemorrhage. The transfusion had no effect on the course of the typhoid as the temperature recurred and the patient went through the ordinary course of the disease from the stage before the hemorrhage occurred. Booth wonders if the transfusion of blood from a donor who had recovered from typhoid would have any beneficial effect upon the course of the disease.

The Treatment of Spirillum Affections of the Mouth with Local Applications of Salvarsan.—ZILZ (*Münch. med. Woch.*, 1912, lix, 20) has had good results with the use of local applications of salvarsan to various non-specific ulcerative conditions of the mouth and in various inflammatory conditions of the gums. He also mentions Vincent's angina as among the conditions that are most favorably influenced by this local treatment with salvarsan. The lesions are thoroughly cleansed with warm physiological salt solution, and salvarsan is applied directly in a 10 per cent. aqueous or glycerin solution, or in an oily suspension. The solutions should be made up fresh, but suspensions in paraffin keep for several days. Zilz says that sluggish ulcers clear up rapidly, and show a tendency to heal. Various forms of spirochetæ that occur in great numbers in many mouth inflammations disappear rapidly under the influence of this local treatment.

Therapeutic Injection of Serum or Defibrinated Blood for Hemorrhage or Anemia.—JOHN (*Münch. med. Woch.*, 1912, lix, 186) reports 6 patients with severe intestinal hemorrhages in the course of typhoid fever apparently cured by injections of defibrinated blood. He draws from 30 to 50 c.c. of blood from a vein in the arm of a healthy person into a glass vessel containing some glass beads. The blood is then defibrinated by vigorously shaking the vessel. He injects the defibrinated blood into the gluteal muscles or subcutaneously. This injection is repeated two or three times at two or three day intervals. John has had equally good results with this method in a case of pernicious anemia. The hemoglobin percentage in this patient had dropped from 38 to 19, and the red cells from 2,200,000 to 600,000 during a month of the usual methods of treatment. This patient received two injections of serum alone. Six weeks after the injections the hemoglobin had risen to 62 per cent., and red cells to 3,500,000. Esch has also reported similar results in 2 cases of pernicious anemia, and he attributes the benefit from the defibrinated blood or serum to a stimulating action of the alien blood on the red bone marrow. John says that when it is difficult to obtain fresh blood, fresh horse serum should be tried in any severe hemorrhage that cannot be controlled by the usual measures.

Codeonal, a New Hypnotic and Sedative.—GAUPP (*Berl. klin. Woch.*, 1912, xlix, 306) says that codeonal appears to be a very efficient hypnotic in certain conditions that usually require morphine. Codeonal is a combination of codine and veronal. It is especially applicable in cases where insomnia is due to pain or when there is distressing dyspnea or cough. It is an efficient hypnotic when it is given to replace

a drug to which a patient has become accustomed. Gaupp says there are no untoward symptoms from its use. It is often of advantage to combine codeonal with sodium-veronal, giving the codeonal in a dose of 0.04 grain and the sodium-veronal in a dose of 0.3 grain.

Streptococcus Vaccines in Scarlet Fever Prophylaxis.—WATTERS (*Jour. Amer. Med. Assoc.*, 1912, lviii, 546) was led to try the effect of streptococcus vaccines as a prophylactic measure against scarlet fever by the work of Grabeitschewsky. His method as described consists in the administration of broth cultures of streptococci in doses of about 0.5 c.c., previously killed by heat and phenol. The injections are given about once a week. After using the vaccine in 700 cases he concluded that it had a decided value from a prophylactic standpoint. A number of other Russians arrived at similar conclusions with a trial of this same method. Watters administered a polyvalent vaccine made of a number of different strains of streptococci that were isolated from the throats of scarlet fever patients. The vaccines were given to nurses who were exposed to the disease in scarlet fever wards. The initial dose given was 50,000,000 of the polyvalent streptococci vaccine about two or three weeks before the nurse went on duty in the wards. This injection was usually followed by some local reaction, soreness of the arm, and occasionally by some general manifestations such as headache or malaise. A second dose of 100,000,000 was given a week later, and a third dose of 200,000,000 at the interval of another week. In comparing the effects observed he states that but one very light case of scarlet fever has occurred among the nurses who have received vaccine treatment, while in a considerably smaller group, under identical conditions, 5 developed severe cases of scarlet fever. Watters does not attempt to draw any conclusions from the small number of cases but he thinks that the results of the vaccine treatment were very suggestive and that the method is worthy of further trial.

The Serum Treatment of Hemorrhage and Blood Dyscrasias.—LESCOIER (*New York Med. Jour.*, 1912, xcv, 223) reviews at length the serum treatment of hemophilia and other allied diseases, and draws conclusions as follows: The coagulation time of the blood in hemophilic subjects is greatly shortened by the injection of fresh serum of any species. The sera of the ox and dog should be avoided because they are more apt to produce toxic symptoms. The local application of fresh serum to wounds in patients with delayed coagulation tends to act as a hemostatic. Regular antitoxic sera are less satisfactory than freshly drawn material. The action of serum in accelerating blood coagulation is apparently due to a substitution of active thrombin.

Therapeutic Results of Radium Emanations.—BENCZUR (*Berl. klin. Woch.*, 1912, xlix, 108) reports 60 cases of various diseases treated by radium emanations given by mouth and also by subcutaneous injections. The treatment was given during a period of from four to eight weeks. The amount given daily was about 1000 Mache units. In 12 cases of tabes the lightning pains were very favorably influenced. The treatment had no effect in 2 cases of tabes who were addicted to the

morphine habit. A number of different forms of neuralgia were much benefited by the radium treatment. Four cases of sciatica were cured; 2 other cases, on the other hand, were not at all influenced by the treatment. The majority of the cases of chronic polyarthritis were also much benefited. The radium emanations seemed to have little or no effect in cases of chronic muscular rheumatism and lumbago. Benzur believes that the curative effect of radium emanations is largely dependent upon the vascular dilatation produced by the remedy, and he has observed a tendency to hemorrhage in a number of the patients during the treatment.

PEDIATRICS

UNDER THE CHARGE OF

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Diphtheria of the Esophagus.—J. D. ROLLESTON (*Brit. Jour. Child. Dis.*, 1912, ix, 12) reports a case of diphtheria of the esophagus in a boy, aged two years. The child when admitted to the hospital was practically moribund from diphtheria involving the nasopharynx and pharynx, with diphtheretic excoriations on one ear and the left malleolus. He had received no antitoxin. Cultures of all the lesions showed the Klebs-Loeffler bacillus. There was marked loss of substance in the left side of the pharynx. The autopsy showed a normal trachea. The esophagus in its upper third was apparently normal, the middle third showed some injection of the mucosa, while in the lower third were two longitudinal areas of necrosis, coalescing below, and about 3.5 cm. in length. The muscular wall was exposed in one area. The diphtheretic membrane had disappeared, but direct smears and cultures showed numerous diphtheria bacilli. This condition is rare, and usually is associated with multiple lesions elsewhere. During life the subsequent development of an esophageal stricture is the only means of making a diagnosis. Mallory reports 251 necropsies in diphtheria in which the above condition was found in 12 cases. In other cases the condition may be due to scarlet fever, since Oppikofer found 15 cases in 128 scarlet fever necropsies. Among cases reported in literature the end results have been perforation of the esophagus, expulsion of the cast with recovery, and the development, subsequently, of an esophageal stricture. In the last named result all cases recovered by gradual dilatation of the stricture by bougies. The frequent use of bougies in strictures from other causes may predispose to diphtheria of the esophagus.

Acute Benzene-poisoning in an Infant.—ADOLPH FRIEDIGER (*Munch. med. Woch.*, 1912, lix, 252) found in literature the reports of 14 cases of poisoning in infants by swallowing benzene. Eight of these died and the others recovered after symptoms of more or less severe intoxication. In but one case was a child reported as poisoned by

inhaling benzine fumes. According to the observations of various authors, benzine exerts a particular toxic effect on the central nervous system, the gastro-intestinal tract, the lungs, and the pleura. Convulsions and vomiting are common and the latter occurs in the inhalation cases also, though less severely. The vomiting of blood and mucus and a diarrhea of the same character occur in cases in which the benzine has been swallowed. The heart action is rapid and irregular and disturbed breathing is common. The temperature rises, in some reported cases to 40.2°C . Loss of consciousness often occurs with great suddenness. Friediger reports his own case of an infant, aged six weeks, which he had been treating for furunculosis complicating an eczema, anemia, and general malnutrition. The infant was much improved and adhesive plaster was being used as a dressing for furuncular areas on the trunk. On one day benzine was employed to loosen the adhesive and cleanse the skin, a fresh adhesive dressing being placed on the various areas. Almost immediately afterward the child became restless, began to vomit, and to have convulsive movements. Within twenty-four hours the child presented absolute pallor, emaciation, expulsive vomiting, convulsions, dyspnea, retracted abdomen, fever, and rapid pulse. It became practically moribund. Immersion in wheat-bran baths and cool sponges improved the condition, and in twenty-four hours the child's condition was good and the toxic symptoms had disappeared. The points of interest in this case are the age of the child (six weeks), and the poisoning by inhalation of fumes from the local application of benzine. Absorption through the skin was possibly a further factor. The case further indicates the danger of the local use of benzine on very young infants with very weak constitutions.

The Eucalyptus Treatment in Scarlet Fever.—E. KOERBER (*Münch. Med. Woch.*, 1912, lix, 581), reports the results obtained by Dr. Rumpel in Eppendorf in testing the eucalyptus treatment in scarlet fever as practised by Milne in England. Milne applies twice daily for the first four days the pure eucalyptus oil to the entire body surface and repeats this once daily for the following six days. He also applies a 10 per cent. solution of carbolic acid in oil to the tonsils every two hours for the first two days. His patients are not isolated and he claims no contagion to unprotected children resulting, either during or after the disease. In an epidemic in Eppendorf the cases were divided as to treatment for the sake of comparison. There were 274 cases treated in the usual manner and 151 with the method of Milne: Infection was transmitted by cases returned to their homes as cured in the following proportions. In 86 cases not treated with eucalyptus oil it occurred 3 times, or 3.5 per cent. In 73 cases treated with eucalyptus oil it occurred 4 times, or 5.5 per cent. Those cases only were reported where the family could be under close observation constantly, thus ruling out infection from other sources. The mortality was only 0.56 per cent. less in the eucalyptus series. It was noteworthy, however, that the complications of endocarditis, nephritis, glandular suppuration, and otitis were 50 per cent. less frequent in the eucalyptus series than under the ordinary treatment. The joint complications however, were more frequent. A shortening of the course of the disease with the eucalyptus treatment was not observed. The period of infectivity

was not shortened, one of the return cases infecting the family three months after the primary onset. Therefore the authors are not convinced of Milne's claims from the above experiences in Eppendorf.

Purpura in Infective Diarrhea.—H. D. ROLLESTON and J. B. MOLONY (*Brit. Jour. Child. Dis.*, 1912, ix, 1) analyzed 100 cases of infective diarrhea in infants to determine the frequency of symptomatic purpura in this disease. Of the 100 cases, averaging infants from seven to eighth months and of both sexes, 67 proved fatal. Of the 67, 16.4 per cent. showed purpura. None of the purpuric cases showed edema. The abdomen and thorax is the frequent site of the purpuric eruption, though the arms and legs are occasionally involved. The hemorrhages are usually small, but may be so closely set as to make the abdomen appear uniformly purple from a distance. The purpura was usually a late symptom and appeared about the thirty-fourth day, a week before death. Occasionally the hemorrhages came out in crops. Transfusion and the administration of horse or other serum seemed to have no influence in causing purpura. In one case only was there evidence of infantile scurvy. No close relation is suggested between purpura and the edema sometimes seen in infective diarrhea. The prognosis appears extremely grave, as all the cases mentioned above died. Voelcker, however, says it is by no means a necessarily fatal sign. To conclude, symptomatic purpura in infective diarrhea mainly occurs on the abdomen and chest of infants under one year of age. It is usually a terminal phenomenon in prolonged cases, and the prognosis is extremely grave.

Drunkards' Children among the Weaklings at School.—EUGEN SCHLESINGER (*Münch. Med. Woch.*, 1912, lix, 649), reporting his observations on weak and backward school children, states that the two important factors in the inherited low resistance and organic weakness of many children are, first, a neuro-psychopathic constitution of the parents, and second, alcoholism in the parent. Next in importance and frequency is syphilis. Out of 200 weaklings studied, Schlesinger found 30 per cent. who were the children of drunkards. A percentage of 40 to 60 was found in severe intellectual weakness, in imbecility, and idiocy. The low vitality found in drunkards' children is traced back to the female parent. Sullivan and Arrivé state that 55 per cent. of the children of alcoholic mothers die either at birth or within two years. The extent of the degeneration in the children can be gauged by their constitution. Only 33 per cent. of them were in good constitution, 57 per cent. only fair, and 9 per cent. very poor. These unfortunate children show nutritional disturbances, catarrh of the respiratory tract, and especially lowered immunity to infections from their first year of life. The most intense and destructive effects of this heredity are seen in the central nervous system, especially the motor side, resulting in convulsive attacks, tic, and epilepsy. While defective intelligence was probably not more marked in the drunkards' children than in other defectives, the psychic, ethical, and moral defectiveness was well marked and combined with an unstable, mercurial temperament. A tendency toward alcoholism is often observed in the offspring of alcoholics. The future of such children is unpromising and an early severing of home associations and strict disciplinary schooling is imperative.

O B S T E T R I C S

UNDER THE CHARGE OF

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Tuberculosis and Pregnancy.—CRISOTOFOLETTI and THALER (*Monats. f. Geburts. u. Gynäk.*, 1911, Band xxxiv, Heft 5) give the results of their clinical observations in experimental researches on this subject, from Schauta's clinic in Vienna. As regards the frequency of this complication, it is usually stated that pregnancy exercises a practically fatal influence over tuberculosis in from 20 to 50 per cent. of all tuberculous women who conceive. In view of this fact it becomes of the greatest importance to ascertain what is the duty of the obstetrician regarding the interruption of pregnancy. The fact that pulmonary tuberculosis usually begins in the apices explains the fatal influence of pregnancy, as pregnancy lessens the expansion of the lungs and interferes considerably with pulmonary circulation. Another factor of importance is the changes in the connective tissue of the lungs and epithelia and the respiratory tract which usually accompany gestation. To disturb the metabolism of pregnancy further complicates the situation. In some cases the inspiration of infectious secretion during actual labor to healthy portions of the lung aids in spreading the tuberculous process. From this and other causes it follows that tuberculosis is most increased during the second half of pregnancy. When the blood serum of the pregnant patient and that of the non-pregnant is studied, one is unable to demonstrate any essential difference which should materially influence the tubercle bacillus. It is thought by Hofbauer and Stern that an indirect relation exists between the lipoid condition of pregnancy and the spread of tuberculosis. It is also thought that the pregnant condition in this regard tends to increase the virulence of the tubercle bacillus. There are many conditions peculiar to pregnancy in disturbed metabolism which are favorable for the development of infection. When the question of the interruption of pregnancy is considered, it is thought that in advanced gestation the interruption of pregnancy exposes the patient to greater danger than spontaneous labor and the puerperal period. The removal of the pregnant uterus in the second half of gestation would certainly inflict as great trauma as parturition. The prolonged interference necessary for the induction of labor is also unfavorable. As regards sterilization of tuberculous patients during the second half of pregnancy by the removal of a portion of the Fallopian tubes, this operation is much more favorably undertaken in the first three or four months of gestation. Where pregnancy has been interrupted the patient is exposed to great danger should conception speedily recur. The use of the x-rays to produce sterility has not been proved of definite value. It is believed that where pregnancy is to be interrupted the contents of the uterus should be removed, fol-

lowed by operation upon the tubes by vaginal incision. In 41 cases this procedure resulted successfully. The effort is made to operate practically outside the peritoneum by traction upon the uterus and round ligaments with tenaculum forceps, making it feasible to secure the insertion of the tube in the peritoneal wound. The excision of a considerable part of the tube at the isthmus is efficient. This method, however, should be limited to the early months, and should not be performed later than the third month. After this time general narcosis is necessary, and pure chloroform is given where there is much expectoration, or lumbar anesthesia is selected. By experiment upon animals, it is found that guinea-pigs from which the ovaries have been removed show a lessened tendency to the spread of tuberculosis, although such animals often show less resistance to a primary infection.

Ectopic Pregnancy Twice in the Same Patient in Six Months, Necessitating Two Laparotomies.—OLIVER (*Brit. Med. Jour.*, December 23, 1911) reports the case of a patient in her second pregnancy, seven weeks advanced, suddenly seized with severe pain in the lower abdomen, and a hemorrhagic discharge. Although operation was not performed for nearly a month there was a continuous vaginal hemorrhage, and three separate attacks of pain. On examination the uterus was not enlarged, and a small swelling was found in the lower portion of the abdomen, with great tenderness. At operation the omentum and intestine was adherent to a swelling in the left posterior segment of the pelvis. On separating the adhesions dark blood immediately escaped. The left tube and ovary were removed, the tube containing an embryo of six or seven weeks, with a quantity of blood clot. Menstruation returned two months after operation, and was normal. The next period was missed, followed by slight pain in the abdomen, with vaginal hemorrhage. A month later, on palpating the abdomen there was slight tenderness in the right iliac region, the body of the uterus was not enlarged, and behind the uterus to the right was a small dense, movable swelling, slightly tender. At the second operation the small intestine was extensively adherent to the tumor. The hematoma burst as soon as grasped, and the right tube and ovary were removed. The tube contained an embryo about three-eighths of an inch in length. The patient made an uninterrupted recovery.

Changes in the Quantity of Blood in Pregnancy, Labor, and the Puerperal Period.—FRIES (*Zeits. f. Geburts. u. Gynäk.*, 1911 Band lxi, Heft 2,) has conducted a series of experiments to ascertain what variation, if any, takes place in the quantity of blood in pregnancy, parturition, and the puerperal period. He finds that during pregnancy a slight diminution in the relative quantity of blood, as compared to the body weight, takes place. During labor and the puerperal period this is succeeded by a gradual rise to the normal, while the quantity of blood, in proportion to the body weight, is often considerably increased in contrast to a loss of body weight at this time. These facts are interesting in connection with pathological conditions occurring during pregnancy, such as eclampsia, heart lesions, unusual plethora, or anemia.

GYNECOLOGY

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Artificial Occlusion of the Ureter.—It occasionally becomes necessary during operations for malignant conditions of the lower abdomen, to resect a considerable portion of a ureter that reimplantation into the bladder, or direct suture of the cut ends, is out of the question. Among the various ways of dealing with this situation one of the simplest, at least theoretically, is that of throwing the corresponding kidney out of function by occluding the ureter. That this is not always so simple as it seems, however, was pointed out by Stoeckel in a paper recently reviewed in these pages. At Stoeckel's suggestion, therefore, a series of experiments to determine the best method of accomplishing this result have been carried out on animals by KAWASOYE (*Zeit. f. gyn. Urologie*, 1912, iii, 113). He tested the occluding effect on the severed ureter of four methods of procedure: (1) Simple ligation, (2) the formation of a two-limbed, U-shaped kink, the two limbs being tightly tied together, (3) the formation of a three-limbed, Z-shaped kink, the three parallel limbs being sewed together with catgut, and a simple ligature in addition being thrown around the ureter distal to the kink, (4) the formation of a true knot in the ureter, distal to which a simple ligature was placed. Only the last of these methods has proved trustworthy in causing complete occlusion of the ureter. This is due to the fact that in all ligation methods in which stasis of the urine or dilatation of the ureter occurs immediately above the ligature the latter in every case breaks into the lumen, with the formation of a fistula or abscess, even though great care be taken not to injure the wall in applying the ligature. The true occlusion of the lumen, due to organization, which occurs below the ligature is hence of no avail. A *sine qua non*, therefore, for the production of a satisfactory occlusion is the introduction of a kink *between* the ligature and the portion of the ureter which is to undergo dilatation, and this kink must be produced without the use of ligatures or sutures, conditions which are best fulfilled by tying the ureter in a knot. This allows at most so little urine to trickle through that the ligature placed about the ureter below it is subjected to no pressure, and is able, without breaking through, to produce complete obliteration of the lumen by fibrous organization.

Bacteriological Examinations during Gynecological Operations.—With a view to ascertaining the bacteriologic conditions that may exist in the abdominal wound and in the peritoneum during various classes of operations, and especially in order to determine the importance of so-called "endogenous infection," BAUEREISEN (*Zentralbl. f. Gyn.*, 1912, xxxvi, 386) has been for a long time taking systematic cultures during the course of his operations. This is done by means of small, sterile

swabs, which are immediately placed in bouillon, from which aerobic and anaerobic blood-agar plates are made after twenty-four hours. He reports the results obtained in 340 cases; 254 of these were laparotomies, the remainder various procedures, largely extensive vaginal operations. The peritoneum was found sterile in but 80 of the 254 laparotomies, and in but 11 of 42 vaginal hysterectomies. Infection was found present especially frequently in carcinoma cases, the peritoneum being found free of organisms in only 2 out of 43 abdominal operations for this condition, and in none of 3 vaginal ones. The abdominal wound was found sterile throughout the operation in only 30 cases. Bauereisen believes that while "endogenous organisms" exist very often, they play an important role only in carcinoma cases, in which they can remain virulent, owing to the favorable cultural conditions furnished by the large area of tissue of poor resistance left after the radical operation. He believes that the vaginal secretion should always be considered unsterile and dangerous, and that the vagina should therefore be thoroughly disinfected before every gynecological operation. To him, "autoinfection," surgically considered, means merely the artificial infection of the wound, during operation, by endogenous organisms. He has attempted to find some means of establishing a more or less certain prognosis from the bacteriologic findings during operation, but has been unable to do this, since bacteriologic methods do not as yet enable us to distinguish with certainty between virulent and avirulent organisms, nor to measure in any accurate way the important factor of the resistance of the patient. Bauereisen says that by carefully protecting the edges of the abdominal wound from every possible contact with the contents of the peritoneal cavity, he has been able to produce a marked reduction in the number of infected wounds, this being especially striking in the carcinoma cases. Using a sheet of "Billroth-battist" over the abdomen, which is incised at the operation, and is fastened exactly to the wound surfaces by means of the Stoeckel speculum, he has attained in many instances healing *per primam*, notwithstanding the presence of large numbers of microorganisms in the peritoneum. This, he thinks, is so far the most tangible result of his bacteriologic studies, but he also considers such examinations of great value in enabling an operator from time to time to control his entire aseptic technique.

Surgical Treatment of Polycystic Kidney.—ROVSING (*Amer. Jour. Urology*, 1912, viii, 120) reports a series of 3 cases of this disease in which distressing symptoms were greatly relieved, and the life of the patients apparently prolonged, by exposing the more affected kidney and performing multiple punctures of the cysts. Since the condition is practically always bilateral, nephrectomy is, except in rare instances, positively contraindicated, and yet severe pain, oliguria, and other severe symptoms demand intervention. Rovsing's first case was a male, aged forty-one years, who suffered from severe pains in the left kidney region. The organ was found at operation to be 18 cm. in length, nodular, and multicystic. First the superficial and then the deeper cysts were punctured, no hemorrhage resulting. The kidney, thus reduced to half its former size, was replaced, and a gauze drain soaked in silver nitrate introduced into the wound. For three days there was a slight discharge of urinous fluid into the dressing, but this then ceased; there was no permanent fistula formed, and no extension of the kidney

tumor into the perirenal tissue, both of which eventualities had been feared by Rovsing. The patient was entirely relieved of his pain; his urinary output increased from 1500 c.c. before operation to 2000 c.c. after, and he lived three years, finally dying of uremia following a fever. The second and third cases were women, aged about fifty years, who presented similar symptoms, and were treated in the same manner. In the second case albuminuria was present; after operation the albumen was greatly reduced in amount, the urinary output tripled, and the urea excretion doubled. In the third case the urinary output was increased from 440 c.c. before operation to 1250 c.c. after, and the urea excretion was increased eight fold. In both these cases also the pain entirely disappeared. Rovsing explains these phenomena on the ground that in polycystic kidney disease normal renal tissue is present between the cysts, but its action is inhibited by pressure; when this is relieved, normal kidney function is reestablished, and the general condition of the patient thus improved. He does not claim that the procedure is more than palliative, but believes that it is of value in relieving symptoms and prolonging life. In an article upon the same subject, BALFOUR (*Journal-Lancet*, 1912, xxxij, 170) reports 2 cases from the Mayo clinic which were treated along similar lines. The first case was that of a woman, aged forty-seven years, in whom at operation one kidney was found to contain a cyst the size of the adult head; the remainder of that kidney, and the kidney of the opposite side, were filled with cysts of all sizes up to that of an orange. In this instance the large cyst only was opened, emptied of about a quart of fluid, and then partially enucleated. The remainder of the sac was sutured to a stab wound, and drainage introduced, but no fluid came away. The patient made an uneventful recovery. In the second case there was a preceding history of injury, which had led to the diagnosis of rupture of the kidney. At operation, however, a cystic kidney was found, the cysts varying in size from that of a pea up to a grape-fruit. The larger cysts were opened and emptied of their contents, reducing the bulk of the organ by three-fourths. Three cigarette drains were introduced, but no fluid whatever came away. This patient likewise recovered.

A New Operation for Retroversio Uteri.—An addition to the long list of operations that have been devised for the treatment of this condition has been made by HEUSNER (*Zentralbl. f. Gyn.*, 1912, xxxvi, 393). He considers the broad ligaments, and especially the cardinal ligaments, which pass through their bases, the most important factors in holding the uterus in its normal anteverted position. Acting on this supposition, he has devised an operation which consists merely in folding together the two broad ligaments behind the uterus, a process which can easily be carried out when they are relaxed. Where the two ligaments meet in the median line posteriorly they are stitched together by a few mattress sutures, thus supporting the uterus in a broad sling, and having much the same relation to that organ that the wings of a bird, folded over its back, have to its body. The ureters remain a finger's breadth below the lowest mattress suture, and are not in any danger; neither are the uterine arteries. Heusner has worked out the operation on the cadaver, and has done it on two patients, with apparently satisfactory results, although sufficient time has not elapsed to judge of the lasting effect.

OTOLOGY

UNDER THE CHARGE OF
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The Fistula Symptom.—G. ALAGNA (*La pratica oto-rino-laringoiatrica*, No. 6, 1911), recognizing the horizontal semicircular canal as the predilective point for penetration of the labyrinth capsule in suppurative middle-ear disease, regards as the best clinical test the alternate rarefaction and condensation of air in the middle ear by means of the Siegle otoscope, or the rarefactor of Delstanehe, firmly inserted into the external auditory canal. The indicative symptoms are usually wanting in children under one year of age, and in patients with an intact vestibular apparatus; the nystagmus, during compression, is directed toward the diseased, and during rarefaction toward the sound side. In cases of chronic suppurative middle-ear disease with positive fistula symptoms and absence of hearing, labyrinth infection may be assumed and operative interference regarded as indicated.

The Influence of Cold Bathing and Swimming upon the Ear and its Diseases.—The establishment of swimming as a part of the customary education of males, in Japan, and the large number of swimming schools, both inland and upon the sea coast, afforded the inducement, as well as the opportunity, for the observations of DR. SHIN, IZI ZIBA (*Arch. f. Ohrenheilk.*, November, 1911). These were made through the medium of the aural clinic of the University of Tokio, when special hearing tests seemed necessary, and were commenced a few days before the usual date for the opening of the swimming schools, which are usually in operation for three months in the year. The material observed consisted of 1916 male individuals ranging from the age of six to thirty years, pupils of the 16 fresh-water and 7 salt-water swimming schools in Tokio. Of this total, the first examination gave 642 individuals with abnormalities detailed in the following list: Cerumen, 469; chronic suppurative middle-ear disease, 61; furunculosis of the external canal, 11; perforation of the drumhead, 40; eicatricial closure of previous perforations, 57; hyperemia of the drumhead, 4; 33.5 per cent. of the whole number examined. The number of cases with ceruminous accumulation was large, as compared with average clinical reports, 73 per cent., the preponderating number being in young children, but in none of these cases was the accumulation occlusive, a fact in accord with the observations of Politzer and Bezold. Next in number came the existent and past cases of suppurative middle-ear disease; the cases in which hyperemia of the drumhead was observed gave no evidence of middle-ear implication. One month after the first observation a second examination of the same material was made, with the resultant addition of 164 patients, 8.5 per cent., to the list,

classified as follows: Cerumen, 330; chronic suppurative middle-ear disease, 61; furunculosis, 302; recurrence of suppurative middle-ear disease, 17; acute middle-ear disease with perforation of the drum-head, 3; open perforation of the drumhead, 29; perforation of the drumhead, cicatricially closed, 51; hyperemia of the drumhead, 10; subjective noises in the ear, 3; in all, 806 cases, 42 per cent. of the total material. The decrease in the number of cases of ceruminous accumulation was apparently due to the effect of water entering the external auditory canal and softening the accumulated mass, or else causing it to swell and occlude the canal, causing impairment of hearing and the application of measures for relief. The increase in the number of cases of furunculosis is especially interesting in the light of the conclusions drawn by Dr. Shin, who refers the frequency of this malady not only to the entrance of water into the external canal and the subsequent irritative and infective efforts at its removal; but also to the favoring influence of exposure to the heat of the sun. It is a matter of common observation in Japan that furunculosis of the ear is more frequent in the sea-beach than in the river swimming schools, 55.1 per cent. of cases in the former, and 41.87 per cent. in the latter, a difference by no means entirely imputable to the more irritative effect of the salt water, since, in the pauses between swims the beach bathers are exposed freely to the rays of the sun, while the river bathers are sheltered by barracks. As a supporting evidence is the fact that 60 per cent. of the cases of furunculosis affected the left ear, the remaining 40 per cent. being right-sided or binaural. In middle Japan right-sided swimming is the preferential exercise, the left side of the body and head being most exposed to the sun; moreover, a further investigation of the swimming habit of the patients with furunculosis of the right ear showed that the majority of them swam upon the left side. It was further found that this frequent malady was much less common among the cases with ceruminous accumulation and much less painful, when it did occur, in consequence probably both of the protection afforded by the accumulated mass and its remedial effect when moistened and swollen. In the cases of subjective noises this symptom was found to be due to a general circulatory rather than to an aural cause, and the hyperemia of the drumhead was usually the result of too prolonged or too forcible local efforts to remove water remaining at the inner end of the canal after the bath. In the comparison drawn between the first and second examination of the cases of chronic suppurative middle-ear disease, Dr. Shin observed no case of deleterious result; the majority of the cases exhibited much greater cleanliness, if not material improvement, as the result of the daily bathing. The recurrent suppurative inflammations of the middle ear were, in all instances, subacute, with an injected drumhead and a mucous or seropurulent discharge, and there were 3 cases of acute perforative middle-ear inflammation in patients whose ears were intact at the first examination; in all of these cases there was furunculosis, and in one of them the injection of the drumhead and the acute middle-ear congestion, with ultimate perforation of the drumhead and a seropurulent discharge, followed the furunculosis. In reference to the question of the frequency of middle-ear implication in swimming by entrance of water through the tympanopharyngeal tube, Dr. Shin is of the opinion that

this does not occur except under unusual causative conditions, entailing considerable variation in air pressure in the nasopharynx, especially sneezing and blowing the nose. As a test in this matter three pupils, with dry persistent drumhead perforations, had the affected ears tightly stopped with plugs of cotton and lard, and then dove five times successively from a springboard, four meters above the water, the middle ears remaining dry. In conclusion Dr. Shin lays stress upon the importance of preliminary and successive aural examinations in all swimming-school pupils, and advises even those with sound ears to use some measure of protection from the possibility of a furuncular infection.

HYGIENE AND PUBLIC HEALTH

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The Purification of Water by Anhydrous Chlorine.—C. R. DARNELL (*Jour. Amer. Pub. Health Assoc.*, November, 1911, i, 783) states that anhydrous chlorine possesses considerable advantages over the hypochlorites, which have been used rather extensively for the purification of water during the last few years. Ordinarily chlorine is introduced into water as hypochlorite of lime. Although the hypochlorite treatment of water has been successful, there are certain disadvantages attending the use of hypochlorites for this purpose. The hypochlorites are unstable compounds and the content of available chlorine is rather uncertain, necessitating frequent chemical examinations in order to determine the quantity to be used. Another objection in the use of hypochlorites is the fact that more or less troublesome dosing devices must be used. It has also been noticed that a relatively slight excess of hypochlorites may impart a disagreeable taste and unpleasant odor to the water. Chlorine is obtained in considerable quantities, at the present time, as a by-product in the manufacture of caustic soda. This chlorine is purified, dried, liquefied by pressure, and placed on the market in steel drums or cylinders. Chlorine so obtained is practically chemically pure, containing merely traces of oxygen, carbon dioxide, and nitrogen. It is necessary in marketing chlorine in this form to remove all water vapor in order to prevent corrosion of the steel used in the construction of the storage drums. The price of this liquefied chlorine varies from ten to fifteen cents per pound. Water at ordinary temperature will absorb about 4000 parts per million, by weight, of chlorine. It will be readily seen that this property of chlorine is of considerable importance in water purification, since it makes it unnecessary to use elaborate mixing devices which would be the case were the

chlorine not so easily soluble. In general it may be stated that an average unfiltered river water will require about one-half of a part, by weight of chlorine gas per million parts of water, to bring about a satisfactory bacterial purification. In other words, it will require from three to four pounds of liquefied chlorine per million gallons of water. Darnell has invented a relatively simple automatic apparatus for the introduction and mixing of chlorine gas with water. This apparatus occupies but a small space, and, judging from the results obtained by its use, is efficient. The important advantages which this method of applying dry chlorine gas has over the use of hypochlorites may be summarized briefly as follows: For cities already having aqueducts and the necessary water supply it is possible to disinfect large amounts of water in a plant occupying little space. A mixing chamber 16 inches in diameter and 24 feet long, for example, has a capacity of 750,000 gallons per day. To purify the water of greater New York, 750,000,000 gallons per day, 16 mixing chambers 10 feet in diameter and 200 feet long would be sufficient. This would occupy about one acre of ground. The cost of labor for operating such a plant would be trifling. The cost of the chlorine would range, roughly speaking, from 35 to 50 cents per million gallons of water. In comparing this with other purification methods Darnell points out that anhydrous chlorine and ozone have practically the same efficiency. The chlorine method, however, is cheaper to operate and rather more reliable because there is no complicated electrical machinery necessary. It also requires less labor. When we compare chlorine and hypochlorites, we find that the advantage of chlorine over hypochlorites consists first in the uniform composition of chlorine, contrasting, in a noteworthy manner, with the variability of the hypochlorites; second, in the relatively small amount of apparatus which is required for adding chlorine to the water supply. Finally, in contrasting chlorine and filtration, it may be noted that a chlorine purifying plant is cheaper to install than a filter plant, and it is cheaper to operate because the labor required is much less. It should be stated that in the chlorine method provision must be made for clarifying the water before the chlorine is added, so that it will usually be necessary to have preliminary sedimenting reservoirs or mechanical filters, for the chlorine in no way clarifies a turbid water.

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All communications should be addressed to—

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